=> fil reg FILE 'REGISTRY' ENTERED AT 17:00:24 ON 15 JUN 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 14 JUN 2007 HIGHEST RN 937362-79-3 DICTIONARY FILE UPDATES: 14 JUN 2007 HIGHEST RN 937362-79-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

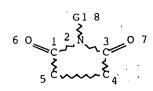
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> d que stat 18

L4 SCR 2043

L6 STR



d@9 Ak@10 Cb@11



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

L8 502 SEA FILE=REGISTRY SSS FUL L6 AND L4

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502 ANSWERS

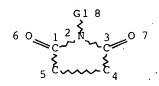
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STEREO ATTRIBUTES: NONE

=> d que stat 121 L21 STR



Id @9 Ak @10 Cb @11



16 S---A E1 17

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STEREO ATTRIBUTES: NONE

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SEL RN

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OR 724722-17-2/BI OR 724722-27-4/BI OR 724722-44-5/BI OR
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L5
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L8
                       502 SEA SSS FUL L6 AND L4
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L18
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L19
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L23
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                            D SCA
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L25
                                    BIOSYNTH?
                              43 SEA ABB=ON PLU=ON L19 AND L25
L26
                              17 SEA ABB=ON PLU=ON L26 AND (1840-2002)/PY,PRY,AY
L27
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L28
                                  AGENT)
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L29
                              29 SEA ABB=ON PLU=ON L27 OR L20 OR L29
L30
                             4 SEA ABB=ON PLU=ON L29 NOT L24
L31
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L32

=> fil hcap

FILE 'HCAPLUS' ENTERED AT 17:01:03 ON 15 JUN 2007

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FILE COVERS 1907 - 15 Jun 2007 VOL 146 ISS 26 FILE LAST UPDATED: 14 Jun 2007 (20070614/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 124 ibib abs hitstr hitind

L24 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:340027 HCAPLUS Full-text

DOCUMENT NUMBER: 140:117092

TITLE: Design and synthesis of pH-responsive polymeric

carriers that target uptake and enhance the intracellular delivery of oligonucleotides Murthy, Niren; Campbell, Jean; Fausto, Nelson;

AUTHOR(S): Murthy, Niren; Campbell, Jean; Fausto, N Hoffman, Allan S.; Stayton, Patrick S.

Hollman, Allan S., Stayton, Fattler S.

CORPORATE SOURCE: Department of Bioengineering, University of

Washington, Seattle, WA, 98195, USA

SOURCE: Journal of Controlled Release (2003), 89(3),

365-374

CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

The delivery of biomol. therapeutics that function intracellularly remains a significant challenge in the field of biotechnol. In this report, a new family of polymeric drug carriers that combine cell targeting, a pH-responsive membrane-disruptive component, and serum-stabilizing polyethylene glycol (PEG) grafts, is shown to direct the uptake and endosomal release of oligonucleotides in a primary hepatocyte cell line. These polymers are called encrypted polymers and are graft terpolymers that consist of a hydrophobic, membrane-disruptive backbone onto which hydrophilic PEG chains have been grafted through acid-degradable linker acetal linkages. In this report, the ability of the encrypted polymers to deliver rhodamine-labeled oligonucleotides or PEG-FITC (a model macromol. drug) (5 kDa) into the cytoplasm of hepatocytes was investigated by fluorescence microscopy. Two new encrypted polymer derivs. (polymers E2 and E3) were synthesized that contained lactose for targeting to hepatocytes. Polymer E2 also has PEG-FITC conjugated to it, as a model macromol. drug, and polymer E3 contains a pendant

hexalysine moiety for complexing oligonucleotides. The results of the fluorescence microscopy expts. show that the encrypted polymers direct vesicular escape and efficiently deliver oligonucleotides and macromols. into the cytoplasm of hepatocytes.

IT 646535-00-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(design and synthesis of pH-responsive polymeric carriers that target uptake and enhance the intracellular delivery of oligonucleotides)

RN 646535-00-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-(2-mercaptoethyl)-ω-hydroxy-, ether with N2-[6-[3-[(2-hydroxyethyl)thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxohexyl]-L-lysyl-L-lysyl-L-lysyl-L-lysine (9CI) (CA INDEX NAME)

1T 646535-00-4DP, reaction products with acrylic polymer derivative
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL
(Biological study); PREP (Preparation); USES (Uses)
 (design and synthesis of pH-responsive polymeric carriers that
 target uptake and enhance the intracellular delivery of
 oligonucleotides)

RN 646535-00-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-(2-mercaptoethyl)-ω-hydroxy, ether with N2-[6-[3-[(2-hydroxyethyl)thio]-2,5-dioxo-1pyrrolidinyl]-1-oxohexyl]-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysine (9CI) (CA INDEX NAME)

$$\begin{array}{c} O & CO2H \\ O & C-NH-CH-(CH_2)_4-NH_2 \\ O & C-NH-CH-$$

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 35

ΙT 2127-03-9P 646534-98-7P 646534-99-8P 646**535-00-4P** 

646535-01-5P 646535-02-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(design and synthesis of pH-responsive polymeric carriers that:

target uptake and enhance the intracellular delivery of oligonucleotides)

646535-00-4DP, reaction products with acrylic polymer derivative IT 646535-01-5DP, reaction products with acrylic polymer derivative

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(design and synthesis of pH-responsive polymeric carriers that target uptake and enhance the intracellular delivery of oligonucleotides)

THERE ARE 22 CITED REFERENCES AVAILABLE REFERENCE COUNT: FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

## => d 129 ibib abs hitstr hitind 1-4

L29 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

2004:1060761 HCAPLUS Full-text ACCESSION NUMBER:

142:36914 DOCUMENT NUMBER:

Multivalent ligands comprising signal

recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector

molecules

Kiessling, Laura L.; Griffith, Byron R.;

Gestwicki, Jason E.; Strong, Laura

PATENT ASSIGNEE(S): USA

U.S. Pat. Appl. Publ., 76 pp., Cont.-in-part of

U.S. Ser. No. 815,296.

CODEN: USXXCO

Patent

DOCUMENT TYPE:

English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004248801		20041209	US 2004-806056	200403
1. 大学工作的现在分词	•			22
US 2003125262	A1	20030703	< US 2001-815296	200103
•			<	21
PRIORITY APPLN. INFO.:	; ·	•	US 2000-191014P	P 200003 21
A Barthage for			< US 2001-815296	A2
	•	A. 1		200103 21
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			US 2003-456778P	P 200303

This invention provides multivalent ligands which carry or display at least one AB recognition element (RE), and preferably a plurality of recognition elements, for binding directly or indirectly to cells or other biol. particles or more generally by binding to any biol. mol. The multivalent ligands provided can most generally function for binding or targeting to any biol. particle or mol. and particularly to targeting of cells or cell types or viruses, for cell aggregation and generally for macromol. assembly of biol. macromols. The multivalent ligands of this invention are generally applicable for creating scaffolds (assemblies) of chemical or biol. species, including without limitation, antigens, epitopes, ligand binding groups, ligands for cell receptors (cell surface receptors, transmembrane receptors and cytoplasmic receptors), and various macromols. (nucleic acids, carbohydrates, saccharides, proteins, peptides, etc.). In these scaffolds, the number, spacing, relative positioning and relative orientation of recognition elements can be controlled. Multivalent ligands of this invention can carry or display at least one signal recognition element (SRE), and preferably a plurality of signal recognition elements, and modulate biol. responses in biol. systems. The SRE is selected from an amino acid, peptide, protein, derivatized peptide, epitope, monosaccharide, disaccharide, polysaccharide, nucleic acid, cell nutrient, antigen, small drug-like compound, hapten, antibody or fragment, or cell surface receptor. Multivalent ligands of this invention can carry or display at least one binding recognition element (BRE), and preferably a plurality of binding recognition elements, optionally in combination with one or more SRE, and modulate biol. responses in biol. systems. The invention also relates to methods for aggregating biol. particles and macromols. and for modulating biol. response employing the multivalent ligands provided.

IT 362663-20-5

RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (multivalent ligands comprising signal recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.)

RN 362663-20-5 HCAPLUS

The state of the state of the

CN  $\beta$ -D-Glucopyranoside, 3-mercaptopropyl O-(N-acetyl- $\alpha$ -neuraminosyl)-(2 $\rightarrow$ 6)-O- $\beta$ -D-galactopyranosyl-(1 $\rightarrow$ 4)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 804565-00-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (multivalent ligands comprising signal recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.)

RN 804565-00-2 HCAPLUS

CN Cyclohexanecarboxamide, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-N-[2-[2-[2-[(2-methyl-1-oxo-2-propenyl)amino]ethoxy]ethoxy]ethyl]-, polymer with N-(2,3-dihydroxypropyl)-2-methyl-2-propenamide (9CI) (CA INDEX NAME)

CM , 1

CRN 804564499-6 CMF C22 H33 N3 O6

CM 2

CRN 41601-36-9 CMF C7 H13 N O3

Fluorescent, substances

Hematopoietic precursor cell

Genomic library

Human Immune system
Immunoblotting

IC ICM A61K038-17 ICS C12N015-85 INCL 514012000; 435455000 15-2 (Immunochemistry) Section cross-reference(s): 1, 9 ΙT Biology Muscle (cell; multivalent ligands comprising signal recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.) Metals, biological studies RL: BSU (Biological study, unclassified); BIOL (Biological study) (chelating agent; multivalent ligands comprising signal recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.) Lipids, biological studies IΤ Macromolecular compounds Peptides, biological studies Proteins : RL: ARU (Analytical role, unclassified); BSU (Biological study, 17 34. unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (conjugates, multivalent; multivalent ligands comprising signal recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.) IT Adhesion, biological Agglutination test Animal cell Animal virus Animals Antibiotics Antitumor agents Apoptosis B cell (lymphocyte) Cell activation Cell aggregation Cell migration Cell proliferation Chemotaxis Diagnostic agents . Drugs Endothelium Epithelium Erythrocyte Eubacteria Eukarvota

Immunohistochemistry Immunomodulators Labels Leukocyte Linking agents Lymphocyte Mammalia Neuron Nutrients PCR (polymerase chain reaction) Pathogen Prokaryota Protein sequences Signal transduction, biological Solid phase synthesis supports Stem cell T cell (lymphocyte) (multivalent ligands comprising signal recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.) Enzyme's, biological studies Macromolecular compounds Polyesters, biological studies Polyethers, biological studies Polymers, biological studies RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified): DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (multivalent ligands comprising signal recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.) Antibodies and Immunoglobulins Antigens Biochemical compounds Carbohydrates, biological studies Disaccharides G protein-coupled receptors Glycoconjugates Lipids, biological studies Monosaccharides Nucleic acids Polysaccharides, biological studies Reagents Trisaccharides | | | | Tumor antigens RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (multivalent; multivalent ligands comprising signal recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.) Alcohols, biological studies RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(polyhydric; multivalent ligands comprising signal recognition

ΙT

IT.

11

element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.) 7440-02-0D, Nickel, chelates and conjugates 9003-05-8, IT 11028-71-0, Concanavalin A Polyacrylamide 25087-26-7, 59880-97-6 64364-50-7 204934-16-7, BODIPY Polymethacrvlic acid 804564-97-4 TR 362663-20-5 RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (multivalent ligands comprising signal recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.) 804565-00-2P 804565-03-5DP, hydroxyethylamide/lysine amide. IT derivs. RL: SPN (Synthetic preparation); PREP (Preparation) (multivalent ligands comprising signal recognition element and binding recognition element for regulating cellular responses and designing diagnostic and therapeutic effector mols.) १ . म. र 🚶 निर्मित्रकीकेन हो है किये हैं . ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN L29 ACCESSION NUMBER: 2003:591145 HCAPLUS Full-text DOCUMENT, NUMBER: 139:138724 Integrin targeted imaging agents TITLE: Lanza, Gregory; Wickline, Samuel A.; Harris, Tom INVENTOR(S): Barnes Jewish Hospital, USA; Bristol-Myers PATENT ASSIGNEE(S): Squibb Medical Imaging, Inc. The PCT Int. Appl., 64 pp. SOURCE: 24, CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: The Hammer of the second English · FAMILY ACC. NUM. COUNT: PATENT INFORMATION: . . . . . DATE APPLICATION NO. DATE PATENT NO. KIND WO 2003062198 -20030731 WO 2003-US2380 A2 WO 2003062198 200301 WO 2003062198 - A8 20031106 **A3** 20050804 WO 20.03062198 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

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     ZA 2004006686
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                                              US 2002-351390P
                                                                  P
PRIORITY APPLN. INFO.:
                                                                     200201
                                              WO 2003-US2380
                                                                     200301
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OTHER SOURCE(S): MARPAT 139:138724

Emulsions preferably of nanoparticles formed from high boiling liquid perfluorochem, substances, said particles coated with a lipid/surfactant coating are made specific to regions of activated endothelial cells by coupling said nanoparticles to a ligand specific for  $\alpha\nu\beta3$  integrin, other than an antibody. The nanoparticles may further include biol. active agents, radionuclides, or other imaging agents. Examples are provided of tumor, atherosclerosis and carotid balloon injury MRI using  $\alpha\nu\beta3$  integrin-targeting nanoparticles comprising, in addition to the targeting agent, a gadolinium chelate.

68-11-1, Mercaptoacetic acid, reactions 569328-04-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(integrin targeted imaging and therapeutic agents)

RN 68-11-1 HCAPLUS

CN Acetic acid, 2-mercapto- (CA INDEX NAME)

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ΙT

RN

11/091.024

13

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[2-[[3-(2,5-dihydro-2,5-dihydro-1H-pyrrol-1-y1)-1-oxopropyl]amino]ethyl]-<math>\omega-[[(10R)-7-hydroxy-7-oxido-2,13-dioxo-10-[(1-oxooctadecyl)oxy]-6,8,12-trioxa-3-aza-7-phosphatriacont-1-y1]oxy]- (9CI) (CA INDEX NAME)$ 

PAGE 1-A

$$CH_2 - CH_2 - C - NH - CH_2 - CH_2$$

PAGE 1-B;

IC ICM C07D ...

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 8, 9

IT Lipids, biological studies

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses) (coating; integrin targeted perfluorocarbon-based nanoparticle imaging agents)

IT Polyoxyalkylenes, biological studies

RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(linker; integrin targeted imaging and therapeutic agents)

IT Peptides, biological studies

RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(linkers; integrin targeted imaging and therapeutic agents)

IT 68-11-1, Mercaptoacetic acid, reactions 569328-04-7 569328-06-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(integrin targeted imaging and therapeutic agents)

IT 67-43-6D, Diethylenetriaminepentaacetic acid, gadolinium complexes 22541-19-1D, Gadolinium ion, complexes, biological studies

60239-18-1D, 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic

acid, gadolinium complexes

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(integrin targeted perfluorocarbon-based nanoparticle imaging agents)

L29 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2002:813875 HCAPLUS Full-text DOCUMENT NUMBER: 137:329436

Prodrugs via acylation with cinnamate

March Bridge Co. B. March

TITLE:

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Gilbert, Carl W.; McGowan, Eleanor B.; Black,
INVENTOR(S):
                        Kirby S.; Harper, Gregory T. P.
                        Cryolife, Inc., USA
PATENT ASSIGNEE (S):
SOURCE:
                                                            2. 在門 15.推翻的
                        PCT Int. Appl., 60 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
                        English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                                           APPLICATION NO.
                                                                DATE
    PATENT NO.
                        KIND
                               DATE
                                           WO 2002-US11330
                         Α2
                               20021024
    WO 2002083067
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                         A3
    WO 2002083067
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    US 6774116
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                               20021024
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     AU 2002258764
                                           AU 2002-258764
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   EP 13.95256
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     JP 2005504006
                               20050210 JP 2002-580872
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                                           US 2001-284304P
PRIORITY APPLN. INFO .:
                                                                200104
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                                           US 2001-315782P
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US 2002-66306

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WO 2002-US11330

200204

#12 billing green

AB A prodrug composition containing a cinnamate moiety and a biol. active mol. moiety which can be released by hydrolysis or activated by light is disclosed. The cinnamate moiety can have substituents of various electronically donating or electronically withdrawing groups to modify the cinnamate moiety's elec. properties as well as photo reactivities for the purpose of achieving a proper hydrolysis rate of the acyl bond between the biol. active mol. moiety and the cinnamic acid backbone. The biol. active mol. can be any biol. active agent or diagnostic, for example, a chemotherapeutic such as a paclitaxel, camptothecin, doxorubicin, amethopterin, etoposide, or fluconazole. The prodrug composition can be modified to add a carrier moiety on the prodrug composition for targeting or to facilitate uptake of the drug. The prodrug compns. can be activated with an energy source to release the drug at the desired site. Representative energy sources can be in the form of elec. force, ultrasound, light or radiation of a radioactive material which can be administered either externally or internally. 165942-79-ODP, NR-LU 10, conjugates with paclitaxel derivative IT

and cinnamate linker

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of prodrugs via acylation with cinnamate for drug release by hydrolysis or activation by energy source)

165942-79-0 HCAPLUS RN

CN Immunoglobulin G2b, anti-(human tumor) Fab fragment (mouse monoclonal NR-LU-10 γ2b-chain), disulfide with mouse monoclonal NR-LU-10  $\kappa$ -chain, oxo[[N,N'-[1-(3-oxopropyl)-1,2-(3-oxopropyl)]]ethanediyl|bis[2-mercaptoacetamidato]](4-)-N,N',S,S']technetate(1-)-99mTc conjugate (CA INDEX NAME)

STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

473440-35-6 473440-35-6D, conjugates with

monoclonal antibodies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preparation of prodrugs via acylation with cinnamate for drug release by hydrolysis or activation by energy source)

RN 473440-35-6 HCAPLUS

CN ' [[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1Hcyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy]carbonyl]-2-(benzoylamino)-2phenylethoxy]-2-methyl-1-oxo-1-propenyl]-3hydroxyphenyl]ethylamino]ethyl]amino]-3-oxopropyl]- $\omega$ -[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethoxy]-(9CI) (CA INDEX NAME)

PAGE 1-A

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PAGE 1-B

PAGE 1-C

RN 473440-35-6 HCAPLUS

CN Poly(oxy-1, 2-ethanediyl),  $\alpha = [3-[[2-[[4-[3-[(1R,2S)-1-[(2R,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy[carbonyl]-2-(benzoylamino)-2-phenylethoxy]+2-methyl-1-oxo-1-propenyl]+3-hydroxyphenyl]ethylamino]ethyl]amino]-3-oxopropyl]-<math>\omega$ -[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethoxy]-(9CI) (CA INDEX NAME)

PAGE 1-A

$$\begin{array}{c} O \\ N \\ CH_2 \\ C$$

PAGE 1-B

$$-CH_2-C-NH-CH_2-CH_2-NH-CH_0$$

$$-CH_2-C-NH-CH_0$$

$$-CH_2-C-C-O-CH-C-O$$

$$-CH_2-C-C-O-CH-C-O$$

PAGE 1-C

IC ICM A61K

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 25

IT Radionuclides, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(radiation from; preparation of prodrugs via acylation with cinnamate for drug release by hydrolysis or activation by energy source)

165942-79: OPP, NR-LU 10, conjugates with paclitaxel derivative.

and cinnamate linker

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of prodrugs via acylation with cinnamate for drug release by hydrolysis or activation by energy source)

473440-33-4 473440-34-5D, conjugates with monoclonal antibodies 473440-35-61473440-35-6D, conjugates with

monoclonal antibodies

RI: THU (Therapeutic use); BIOL (Biological study); USES (Uses).

(preparation of prodrugs via acylation with cinnamate for drug release by hydrolysis or activation by energy source)

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L29 ANSWER 4 OF 4 HCAP ACCESSION NUMBER: DOCUMENT NUMBER: TITLE:	2001:5193 135:11197 Diagnosti phospholi	35 HCAPLU 7 .c/therapeu .pid-based	· · · · · · · · · · · · · · · · · · ·	
INVENTOR(S):  PATENT ASSIGNEE(S):	Tolleshau Halldis; Dagfinn;	, Jo; Rong g, Helge;		Hellebust,
SOURCE:	U.S., 89 958,993. CODEN: US	pp., Cont.	-in-part of U.S.	Ser. No.
DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:	Patent English 10	. :		
PATENT NO	KIND DA	TE	APPLICATION NO.	DATE
US 6261537	B1 20	010717	US 1997-960054	199710
CN 1234742	A 19	991110	< CN 1997-199047	29
			<	199710
ни 9904595	A2 20	000428	ни 1999-4595	199710
AT 318618	т 20	060315	< AT 1997-910514	28 199710 28
ES 2264159	т3 20	061216	< ES 1997-910514	199710
EP 1442751	A1 20	040804	< EP 2004-7226	199804
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PT; IE, FI,	CY	·	ES 1998-917461	199804
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	CN 1140010	•	20030910	CN 2002-100420	200212
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US 2003-722075	, A2	
	••	200311
		26

Targetable diagnostic and/or therapeutically active agents, e.g. ultrasound contrast agents, having reporters comprise gas-filled microbubbles stabilized by monolayers of film-forming surfactants, the reporter being coupled or linked to at least one vector. The gas is air, nitrogen, oxygen, carbon dioxide, hydrogen, an inert gas, a sulfur fluoride, selenium hexafluoride, a low mole weight hydrocarbon, a ketone, an ester, a halogenated low mole weight hydrocarbon or

21

their mixts. The film-forming surfactant material is one or more phospholipids selected from the group consisting of phosphatidylserines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids and cardiolipins. A therapeutic agent is an antineoplastic agent, blood product, biol. response modifier, antifungal agent, hormone or hormone analog, vitamin, enzyme, antiallergic agent, tissue factor inhibitor, platelet inhibitor, coagulation protein target inhibitor, fibrin formation inhibitor, fibrinolysis promoter, antiangiogenic, circulatory drug, metabolic potentiator, antitubercular, antiviral, vasodilator, antibiotic, antiinflammatory, antiprotozoal, antirheumatic, narcotic, opiate, cardiac glycoside, neuromuscular blocker, sedative, local anesthetic, general anesthetic or genetic material. For example, an endothelial cell adhesion of phosphatidylserineencapsulated perfluorobutane microbubbles coated with polylysine was higher than adhesion of uncoated microbubbles. Also, a thrombus was detected by ultrasound in patients with suspected venous thrombosis using i.v. phosphatidylserineencapsulated microbubbles. The microbubbles contained inactivated human thrombinsuccinyl-PEG 3400-distearoylphosphatidylethanolamine incorporated into the encapsulating membrane.

IT 62571-86-2, Captopril

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of diagnostic/therapeutic agents having
phospholipid-based gas-filled microbubbles coupled to one or more vectors)

RN 62571-86-2 HCAPLUS

CN L-Proline, 1-[(2S)-3-mercapto-2-methyl-1-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 207403-10-9P 1 1

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of diagnostic/therapeutic agents having phospholipid-based gas-filled microbubbles coupled to one or more vectors)

RN 207403-10-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[6-hydroxy-6-oxido-1,12-dioxo-9-[(1-oxooctadecyl)oxy]-5,7,11-trioxa-2-aza-6-phosphanonacos-1-yl]-  $\omega$ -[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

$$\begin{array}{c|c} CH_2-CH_2-C & NH-CH_2-CH_2-O & CH_2-CH_2-O & NH-CH_2-CH_2-O \\ \hline \\ O & NH-CH_2-CH_2-O & NH-CH_2-CH_2-O & NH-CH_2-CH_2-O \\ \hline \end{array}$$

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PAGE 1-B

IT 207302-63-4P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of diagnostic/therapeutic agents having phospholipid-based gas-filled microbubbles coupled to one or more vectors)

RN 207302-63-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[6-hydroxy-6-oxido-1,12-dioxo-9[(1-oxooctadecyl)oxy]-5,7,11-trioxa-2-aza-6-phosphanonacos-1-yl]ω-hydroxy-, ether with L-arginylglycyl-L-α-aspartyl-S-[1[3-[(2-hydroxyethyl)amino]-1-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]-Lcysteine (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

$$-CH_{2} - CH_{2} -$$

PAGE 1-C

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IC
    ICM A61B008+00
    ICS A61B005-055; A61K051-00; A61K049-04; A61K009-14
INCL 424009520
    63-6 (Pharmaceuticals)
    Section cross-reference(s): 8
    Hormones, animal, biological studies
IT
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
       (and analogs; preparation of diagnostic/therapeutic agents; having
       phospholipid-based gas-filled microbubbles coupled to one or more
       vectors)
    Hydrocarbons, biological studies
ΙT
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (halo; preparation of diagnostic/therapeutic agents having
       phospholipid-based gas-filled microbubbles coupled to one or more
       vectors)
IT
    Hydrocarbons, biological studies
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (low-mol.-weight; preparation of diagnostic/therapeutic agents having
       phospholipid-based gas-filled microbubbles coupled to one or more
      vectors)
    Ketones, biological studies
IT
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (perfluoro; preparation of diagnostic/therapeutic agents having
       phospholipid-based gas-filled microbubbles coupled to one or more
        vectors)
IΤ
    Ethers, biological studies
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (perfluoroalkyl; preparation of diagnostic/therapeutic agents having
        phospholipid-based gas-filled microbubbles coupled to one or more
       vectors)
IT
     Cardiolipins
     Enzymes, biological studies
    Esters, biological studies
     Fibronectins
     Ketones, biological studies
     Peptides, biological studies
     Perfluorocarbons
     Phosphatidic acids
     Phosphatidylglycerols
     Phosphatidylinositols
     Phosphatidylserines
     Vitamins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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        phospholipid-based gas-filled microbubbles coupled to one or more
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     57-88-5, Cholesterol, reactions 75-31-0, Isopropylamine, reactions
IT
     106-89-8, Epichlorohydrin, reactions
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     2-Dimethylaminoethylamine
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     544-77-4, 1-Iodohexadecane
                            4537-76-2, Distearoylphosphatidylethanolamin
     1142-20-7 3303-84-2
         7144-08-3, Cholesteryl chloroformate 14199-15-6, Methyl
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                                 136268-87-6
     109292-46-8
                   125720-21-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of diagnostic/therapeutic agents having
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phospholipid-based gas-filled microbubbles coupled to one or more

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vectors)
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     29121-23-1P 72224-27-2P
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IT
                   120074-77-3P
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    115399-07-0P
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        (preparation of diagnostic/therapeutic agents having
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        vectors)
IT
     57-88-5DP, Cholesterol, conjugates with drugs
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    Streptavidin, reaction products with polyethoxylated phospholipid
    derivative 33276-37-8P 137056-72-5P 148001-65-4P
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     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
      (preparation of diagnostic/therapeutic agents having
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        vectors)
                       58-85-5D, Biotin, reaction products with
IT
     58-85-5, Biotin
     antibodies or oligonucleotides
                                     59-05-2, Methotrexate 76-19-7,
     Perfluoropropane 124-38-9, Carbon dioxide, biological
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     38000-06-5, Poly(L-lysine)
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     Distearoylphosphatidylserine
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               138757-15-0, \alpha2-Antiplasmin
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        phospholipid-based gas-filled microbubbles coupled to one or more ...
        vectors)
                               THERE ARE 49 CITED REFERENCES AVAILABLE
REFERENCE COUNT:
                               FOR THIS RECORD. ALL CITATIONS AVAILABLE Holder
                               IN THE RE FORMAT
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L32 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 2006:231050 HCAPLUS Full-text

DOCUMENT NUMBER: 144:299431

TITLE: Albumin-based colloid composition having at

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least one protected thiol region, methods of
                         making, and methods of use
                         Assaly, Ragheb A.; Dignam, J. David; Shapiro,
                         Joseph I.
PATENT ASSIGNEE(S):
                         Medical University of Ohio At Toledo, USA
SOURCE:
                         U.S. Pat. Appl. Publ., 58 pp., Cont.-in-part of 10
                         U.S. Ser. No. 985,798.
                         CODEN: USXXCO
                         Patent
LANGUAGE:
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                         English,
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     PATENT NO.
                         KIND
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     US 2006057070
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             SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
             IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
             TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
             ZW, AM; AZ; BY, KG, KZ, MD, RU, TJ, TM
                                             US 2002-106793
PRIORITY APPLN. INFO .:
                                                                  200203
                                                                     Fig. 1. Sept.
                                                                 A2
                                             US 2004-985798
                                                                    ,200411
                                                                     09
                                             US 2001-279017P
                                                                    200103
                                             US 2005-258646
```

26

AΒ A composition comprising an albumin-based colloid composition having at least one protected thiol region, method of making the same, and method for use, including treating hypovolemic conditions such as capillary leak syndrome and shock, are disclosed. The composition also is modified with an indicator reagent such as chromophores. An example concerns the use of PEG-modified albumin in sepsis. IΤ

3483-12-3, Dithiothreitol 760175-37-9

RL: RCT (Reactant); RACT (Reactant or reagent) (albumin-based colloid composition having at least one protected thiol region, methods of making, and methods of use)

RN 3483-12-3 HCAPLUS

CN 2,3-Butanedio1; 11,4-dimercapto-, (2R,3R)-rel- (CA INDEX NAME) The Administration

Relative stereochemistry.

760175-37-9 HCAPLUS RN

CN. Poly(oxy-1,2-ethanediyl),  $\alpha-[[3-[2-[2-[2-(2,5-dihydro-2,5$ dioxo-1H-pyrrol-1-yl)ethoxy]ethoxy]ethyl]amino]-1-[2-[[2-[2-[2-(2.5-1)]]ethoxy]ethyl]amino]-1-[2-[[2-[2-[2-(2.5-1)]]ethoxy]ethyl]amino]-1-[2-[[2-[2-[2-(2.5-1)]]ethoxy]ethyl]amino]-1-[2-[[2-[2-[2-(2.5-1)]]ethyl[ethyl]ethyl]ethyl]ethyl[ethyl]ethyl[ethyl]ethyl]ethyl[ethydihydro-2,5-dioxo-1H-pyrrol-1-yl)ethoxy]ethoxy]ethyl]amino]-2oxoethyl]=3-oxopropyl]amino]carbonyl]-0-methoxy- (9CI) INDEX NAME)

PAGE 1-B

$$\begin{array}{c|c}
 & C & CH_2 - CH_2 \\
\hline
 & C & NH - CH_2 - CH_2 - O - CH_2 - CH_2 - CH_2 - O - CH_2 - CH_2 -$$

INCL 424009600; 514002000; 530363000

CC 63-6 (Pharmaceuticals)

Apoptosis ΙT

Burn

Drug delivery systems

ជា ៨៨១៨ ឆ្នាំ នៅជំនាម ខេត្តប្រ

```
Dyes
    Hypoxia, animal
    Oxidative stress, biological
            100
    Shock (circulatory collapse)
    Surgery
       (albumin-based colloid composition having at least one protected thiol
       region, methods of making, and methods of use)
    Albumins, biological studies
ΙT
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
       (deficiency; albumin-based colloid composition having at least one
       protected thiol region, methods of making, and methods of use)
    Albumins, biological studies
IT
    RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study);
    RACT (Reactant or reagent); USES (Uses)
       (human; albumin-based colloid composition having at least one
       protected thiol region, methods of making, and methods of use)
IT
    Albumins, biological studies
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
       (hypoalbuminemia; albumin-based colloid composition having at least
       one protected thiol region, methods of making, and methods of
       use). ....
                               9004-74-4, Methoxy polyethylene
IT
    3483-12-3, Dithiothreitol
            63368+54+7, 5-Iodoacetamidofluorescein 144512-87-8,
                                         174569-25-6
    Tetramethylrhodamine-5-iodoacetamide
                                                       187848-51-7
    292170-95-7 533881-65-1 760175-37-9
  RL: RCT (Reactant); RACT (Reactant or reagent)
      (albumin-based colloid composition having at least one protected thiol
       region, methods of making, and methods of use)
    ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                       2006:37101 HCAPLUS Full-text
DOCUMENT NUMBER:
                       144:129719
                       Hydrolytically stable maleimide-terminated
                       polymers
                       Kozlowski, Antoni; Gross, Remy F., III; McManus, Samuel P.
                       Samuel P.
PATENT ASSIGNEE(S):
                       USA
                       U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of
SOURCE:
                       U.S. Ser. No. 751,274.
                       CODEN: USXXCO
DOCUMENT TYPE:
                       Patent
                                                                    LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:
      12 July 1887 (1997)
                                                              DATE
    PATENT NO.
                                         APPLICATION NO.
                       KIND
                              DATE
     US 2006009590
                        A1
                              20060112
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US 2004204548 A1

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PRIORITY APPLN. INFO.:

20060112	US 2005-91024	•
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20041014	US 2003-751274	and the state of t
		200312
* *		7 - 1 14 <b>31</b>
	<	a de la companya de
	US 2002-437211P	P P
•		200212
		31

US 2003-751274

OTHER SOURCE(S):

MARPAT 144:129719

AΒ The present invention is directed to hydrolytically stabilized maleimidefunctionalized water soluble polymers (e.g., polyethylene glycol derivs.) and to methods for making and utilizing such polymers and their precursors.

IT 60-24-2DP, 2-Mercaptoethanol, conjugate with maleimide-containing polymers 724721-96-4P 724722-20-7DP, conjugate with 2-mercaptoethanol 724722-20-7P 724722-27-4P 724722-47-8DP, conjugate with 2-mercaptoethanol 724722-47-8P 724722-58-1DP, conjugate with 2-mercaptoethanol 724722-58-1P 724722-68-3DP, conjugate with 2-mercaptoethanol 724722-75-2DP, conjugate with 2-mercaptoethanol 724722-75-2P 873292-89-8P

RL: IMF (Industrial manufacture); PREP (Preparation) (hydrolytically stable maleimide-terminated polymers)

RN

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60-24-2 HCAPLUS Ethanol, 2-mercapto- (CA INDEX NAME) CN

но-сн<sub>2</sub>-сн<sub>2</sub>-sн.

724721-96-4 HCAPLUS RN

CN Poly(oxy=1,2+ethanediyl),  $\alpha,\alpha'=[[(1S)-1-[[[2-[[7-(2,5$ dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxoheptyl]amino]ethyl]amino]carb onyl]-1,5-pentanediyl]bis(iminocarbonyl)]bis(ω-methoxy- (9CI) (CA INDEX NAME)

RN

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[15-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxo-6,9,12-trioxa-2-azapentadec-1-yl]-<math>\omega$ -methoxy-(9CI) (CA INDEX NAME)

马根状 网络人名

PAGE 1-A

RN 724722-20-7 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[15-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxo-6,9,12-trioxa-2-azapentadec-1-yl]- $\omega$ -methoxy-(9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

$$-CH_2$$
 OMe

RN 724722-27-4 HCAPLUS

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CN Poly(oxy-1,2-ethanediyl),  $\alpha-[2-[[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]carbonyl]amino]ethyl]-<math>\omega$ -methoxy-(9CI) (CA INDEX NAME)

office to be the second

$$\begin{array}{c|c} O \\ C - NH - CH_2 - CH_2 \\ \hline \\ CH_2 \\ O \end{array} \qquad \begin{array}{c|c} O - CH_2 - CH_2 \\ \hline \\ \\ N \end{array} \qquad \begin{array}{c|c} O \\ \\ O \end{array}$$

RN 724722-47-8 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[3-[[[4-[(2,5-dihydro-2,5-dioxo-lH-pyrrol-1-yl)methyl]cyclohexyl]methyl]amino]-3-oxopropyl]- $\omega$ -methoxy- (9CI) (CA INDEX NAME)

MeO 
$$\begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix}$$
  $CH_2 - CH_2 - CH$ 

RN 724722-47 8 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[3-[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]methyl]amino]-3-oxopropyl]-<math>\omega$ -methoxy- (9CI) (CA INDEX NAME)

MeO 
$$CH_2$$
  $CH_2$   $O$   $CH_2$   $CH_2$   $CH_2$   $CH_2$   $CH_2$   $O$   $O$   $O$ 

RN 724722-58-1 HCAPLUS

沙 医螺旋形 证

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[3-[[(trans)-4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)cyclohexyl]methyl]amino]-3-oxopropyl]-<math>\omega$ -methoxy-(9CI) (CA INDEX NAME)

MeO 
$$CH2-CH2-O$$
  $n$   $CH2-CH2-C-NH-CH2$ 

RN 724722-58-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[3-[[[(trans)-4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)cyclohexyl]methyl]amino]-3-oxopropyl]-ω-methoxy- (9CI) (CA INDEX NAME)

MeO 
$$\begin{bmatrix} CH2-CH2-O \\ \end{bmatrix}$$
  $CH2-CH2-C-NH-CH2$ 

RN 724722-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[3-[[(trans)-4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)cyclohexyl]amino]-3-oxopropyl]-ω-methoxy-(9CI) (CA INDEX NAME)

MeO 
$$CH2-CH2-O$$
  $ROUND CH2-CH2-C-NH$ 

RN 724722-75-2 HCAPLUS

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CN Poly(oxy-1,2-ethanediyl), α-[3-[[[3-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]methyl]amino]-3-oxopropyl]-ω-methoxy-(9CI) (CA INDEX NAME)

MeO 
$$CH_2$$
  $CH_2$   $O$   $CH_2$   $CH_2$   $CH_2$   $CH_3$   $CH_4$   $CH_5$   $CH_5$   $CH_6$   $CH_6$   $CH_6$   $CH_7$   $CH_8$   $CH_8$   $CH_9$   $CH_9$ 

RN 724722-75-2 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[3-[[[3-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]methyl]amino]-3-oxopropyl]- $\omega$ -methoxy- (9CI) (CA INDEX NAME)

$$MeO = \begin{bmatrix} CH_2 & CH_2 &$$

RN 87,3292-89-8 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[15-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1,12-dioxo-5,8-dioxa-2,11-diazapentadec-1-yl]- $\omega$ -methoxy- (9CI) (CA INDEX NAME)

PAGE 1-B

INCL 525374000; 525056000

CC 37-3 (Plastics Manufacture and Processing)

Section cross-reference(s): 6

IT 60-24-2DP, 2-Mercaptoethanol, conjugate with

```
maleimide-containing polymers 724721-96-4P
                                             724722-06-9P
724722-12-7P 724722-20-7DP, conjugate with
2-mercaptoethanol 724722-20-7P 724722-27-4P
724722-44-5P 724722-47-8DP, conjugate with
2-mercaptoethanol 724722-47-8P 724722-58-1DP,
conjugate with 2 mercaptoethanol 724722-58-1P
724722-68-3DP, conjugate with 2-mercaptoethanol
724722-75 2DP, conjugate with 2-mercaptoethanol
724722=75-2P 873292-89-8P
RL: IMF (Industrial manufacture); PREP (Preparation)
   (hydrolytically stable maleimide-terminated polymers)
```

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L32 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:985312 HCAPLUS Full-text
                         143:292535
DOCUMENT NUMBER:
                         Releasable polymeric drug conjugates based on
                         biodegradable linkers
                         Zhao, Hong; Greenwald, Richard B.; Adler, Susan
INVENTOR (S):
                         USA
PATENT ASSIGNEE(S):
                         U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of
SOURCE:
                         U.S. Ser. No. 449,849.
                         CODEN: USXXCO
                         Patent
DOCUMENT TYPE:
                         English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
        Carry Mar 1916
                                            APPLICATION NO.
     PATENT NO.
                         KIND
                                            US 2004-11818
                                20050908
                          Α1
     US 2005197290
                                                                   200412
     US 2004037802
                                            US 2002-218167
                                20040226
                                                                   200208
                           B2
                                 20061017
      US 7122189
                                             US 2003-449849
                                 20050106
                           A1
      US 2005003448
                                                                    200305
                                                                   30
                 B2
                                 20060808
      US 7087229
                                             WO 2005-US45467
     WO 2006066020
                                 20060622
                           A2
                                                                  200512
        1.45 写型的现代
                                 20060810
     WO 2006066020
                           Α3
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
              CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
              GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
             KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG,
              MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT,
              RO, RU; SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
          IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR,
               BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
            TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
               ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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PRIORITY APPLN. INFO.:

US 2002-218167

200208 13

US 2003-449849

200305

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US 2004-11818

200412

14

OTHER SOURCE (S): MARPAT 143:292535

Disclosure is activated polymeric bicine derivs., as well as conjugates made therewith. Methods of making and using the bicine derivs. are also disclosed. AB For example, antitumor prodrugs of PEG conjugated with doxorubicin through amide linker was prepared

96-53-7, 2-Mercaptothiazoline IT

RL: RCT (Reactant); RACT (Reactant or reagent) (releasable polymeric conjugates based on biodegradable linkers)

96-53-7 HCAPLUS RN

2-Thiazolidinethione (CA INDEX NAME) CN

864159-23-9 864159-24-0 IT

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (releasable polymeric conjugates based on biodegradable linkers)

864159-23-9 HCAPLUS

RN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[28-(2,5-dihydro-2,5-dioxo-1H-CN pyrrol-1-yl)-1,12,16,24-tetraoxo-20-[2-oxo-2-(2-thioxo-3thiazolidinyl)ethyl]-5,8,14,17,23-pentaoxa-2,11,20-triazaoctacos-1 $y1]-\omega$ -methoxy- (9CI) (CA INDEX NAME)

-СH2—О—СH2—С -NH-CH2-CH2-O-CH2-

Poly(oxy-1,2-ethanediyl),  $\alpha$ -[28-(2,5-dihydro-2,5-dioxo-1H-CN pyrrol-1-yl)-1,12,16,24-tetraoxo-20-[2-oxo-2-(2-thioxo-3thiazolidinyl)ethyl]-5,8,14,17,23-pentaoxa-11,20-triazaoctacos-1-yl]ω-methoxy- (9CI) (CA INDEX NAME)

$$-CH_2 - O - (CH_2)^3 - C - O - CH_2 - CH_2 - O - OH_2 - CH_2 - OH_2 -$$

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ICM A61K038-17 ICS C07H015-24; A61K031-325

INCL 514012000; 514483000; 560159000; 514034000; 530409000; 536006400

63-6 (Pharmaceuticals)

, and a first of a first

Section cross-reference(s): 21, 35

75-36-5, Acetyl:chloride 96-53-7, 2-Mercaptothiazoline IT619-60-3, DMAP 4480-83-5, 1,4-Dioxane-2,6-dione 7087-68-5; Diisopropylethyl amine 9001-63-2, Lysozyme 23214-92-8, 153086-78-3 Doxorubicin 25322-68-3, PEG 42503-45-7 864159-13-7

RL: RCT (Reactant); RACT (Reactant or reagent) (releasable polymeric conjugates based on biodegradable linkers).

62304-98+7D; Thymosin  $\alpha1$  (cattle), polyoxyethylenated 864159-21-7 864159-20-6 conjugate derivs. 864159-19-3 864159-22-8, 864159-23-9 864159-24-0 864159-25-1D, peptide conjugate derivs.

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (releasable polymeric conjugates based on biodegradable linkers)

L32 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN 2004:964831 HCAPLUS Full-text ACCESSION NUMBER:

141:410944 DOCUMENT NUMBER:

Preparation of piperidinyl targeting compounds that selectively bind integrins

De Corte. Bart; Kinney, William A.; Maryanoff,

Bruce E.; Ghosh, Shyamali; Liu, Li . Tall to Tiple

PATENT ASSIGNEE (S):

U.S. Pat. Appl. Publ., 160 pp., Cont.-in-part of

U.S. Ser. No. 641,964. CODEN: USXXCO

DOCUMENT TYPE:

INVENTOR(S):

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

Patent

English

	PATENT, NO	KIND	DATE	APPLICATION NO.	DATE
	US 2004224986	<b>A</b> 1	20041111	US 2004-782060	
	5 5 6 6 4 7 1 4 5				.200402
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•	US 2004077684	:A1	20040422	US 2003-641964	200208
	en in sylveria (avyl) in in its a		30 1	4.4	200308
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	AU 2004316476	A1	20050909	AU 2004-316476	
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	CA 2556768	A1	20050909	CA 2004-2556768	200403
		1 '			200403
	WO 2005082889	A1	20050909	WO 2004-US9465	Committee Committee Committee
			5 1		200403
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				BA, BB, BG, BR, BW,	
				DK, DM, DZ, EC, EE,	
				ID, IL, IN, IS, JP, LU, LV, MA, MD, MG,	
				PG, PH, PL, PT, RO,	
				TN, TR, TT, TZ, UA,	
	VC, VN, YU,	ZA, ZN	1, ZW		The state of the s
				SD, SL, SZ, TZ, UG,	
				TM, AT, BE, BG, CH,	
				HU, IE, IT, LU, MC, CF, CG, CI, CM, GA,	
	ML, MR, NE,			01, 00, 01, 011, 011,	
	EP 1718635	A1	20061108	EP 2004-749482	
			,		200403
		1.	. 50 55	OD OD TM 17 111	29
	R: AT, BE, CH,	DE, DI	K, ES, FR,	GB, GR, IT, LI, LU, MK, CY, AL, TR, BG,	CZ FF HIT HIT CAN
	PL, SK	тт, т,	/, F1, RO,	MR, CI, AL, IR, BG,	CZ, EE, HO,
	IN 2006KN02400	A	20070525	IN 2006-KN2400	
•					200608
		_	22261115	NO 2006 4212	24
	NO 2006004212	A	20061115	NO 2006-4212	200609
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PRIO	RITY APPLN. INFO.:	* *		US 2002-404239P	P
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		•		US 2003-641964	<b>A2</b>
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				US 2004-782060	A 200402
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				· · · · · · · · · · · · · · · · · · ·	4.9

OTHER SOURCE(S):

MARPAT 141:410944

GΙ

$$(CH_2)q$$
  $R_2$   $(CH_2)q$   $R_2$   $(CH_2)q$   $R_2$ 

The present invention relates to the synthesis and biol. application of AB piperidinoyl carboxylic acid integrin antagonists affinity moiety of formula (I) and formula (II) [W = -C0-6alkyl(R1), -C1-6alkyl(R1a), -C0-6alkylaryl(R1,R8), -C0-6alkylaryl(R1,R8)]C0-6 alkylheterocyclyl(R1,R8), etc.; R1 = H, (un)substituted NH2, -heterocyclyl-(R8), -heteroaryl-(R8); Rla = -C(R4)(:NR4), -C(:NR4)-N(R4)2, -C(:NR4)-N(R4)(R6), -C(:N-R4)-N(R4)-C(O)-R4, etc.; R4 = H, C1-8 alkyl; R8 = H, -C1-8 alkyl(R9), -CHO, -CO-C1-8 alkyl(R9), -CONH2, etc.; R9 = H, C1-8 alkoxy, each (un)substituted NH2, CONH2, or SO2NH2, CHO, etc.; q = 0-3; R2 = -C1-8 alkyl(R7)(R11), -C2-8alkenyl(R7)(R11), -C2-8 alkynyl(R7)(R11), -cycloalkyl-(R7)(R11), -heterocyclyl-(R8)(R12), etc., R7 = H, -C1-8 alkoxy(R9), each (un)substituted NH2 or CONH2, CHO, -CO-C1-8 alkyl(R9), etc.; R11 = -C1-8 alkyl(R14), -O-C1-8 alkyl(R14), -NH-C1-8 alkyl(R14), -S-C1-8 alkyl(R14), etc.; R12 = -C1-8 alkyl(R14), -O-C1-8 alkyl(R14), -NH-C1-8 alkyl(R14), etc.; R14 when R11 and R12 terminates with a C(:0) is selected from the group consisting of H, OH, -OC1-4 alkyl, and NH2; otherwise R14 = OH, SH, CO2H, CO2-1-4 alkyl; Z = OH, (un)substituted NH2, -O-C1-8 alkyl, O-C1-8 alkyl-OH, -O-Cl-8 alkyl-Cl-8 alkoxy, etc.] and pharmaceutically acceptable salts, racemic mixts., and enantiomers thereof. These affinity moieties maybe used with imaging agents or liposomes to target cells that express the  $\alpha v \beta 3$ ,  $\alpha v \beta 5$ , or  $\alpha v \beta 6$ integrin receptors. For example, an enantiomer of 6-methoxy- $\beta$ -[[1-[1-oxo-3-(5,6,7,8- tetrahydro-1,8-naphthyridin-2-yl)propyl]-4-piperidinyl]methyl]-3pyridinepropanoic acid inhibited the binding of vitronectin to ανβ3, ανβ5, and  $\alpha$ IIb $\beta$ 3 receptors with IC50 of 0.0003±0.00002, 0.0042±0.0018, and 1.83±0.57  $\mu$ M, resp.

IT 791821-41-5P

CN

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of piperidinealkanoic acids as cell targeting compds. with selective affinity to  $\alpha \nu \beta 3$  ,  $\alpha \nu \beta 5$  , or

 $\alpha v \beta 6$  integrin receptors for use with imaging agents or liposomes)

791821-41-5 HCAPLUS RN

4-Piperidinebutanoic acid,  $\beta$ -[4-[2-[2-(2mercaptoethoxy)ethoxy]ethoxy]-3-methoxyphenyl]-1-[1-oxo-3-(1,5,6,7tetrahydro-1,8-naphthyridin-2-yl)propyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

-O-CH2-CH2-SH

791821-38-0P 791821-43-7P IT

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of piperidinealkanoic acids as cell targeting compds. with selective affinity to  $\alpha v \beta 3$ ,  $\alpha v \beta 5$ , or

 $\alpha v \beta 6$  integrin receptors for use with imaging agents or liposomes)

791821-38-0 HCAPLUS RN

4-Piperidinebutanoic acid,  $\beta$ -[4-[2-(2-mercaptoethoxy)ethoxy]-3-CN methoxyphenyl]-1-[1-oxo-3-(1,5,6,7-tetrahydro-1,8-naphthyridin-2yl)propyl]- (9CI) (CA INDEX NAME)

, a ja je venik ind -CH2--CH2--SH

and the state of the 791821-43-7 HCAPLUS RN

(carboxymethyl)-2-[1-[1-oxo-3-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-(1,5,6,7-tetrahydro-1,8-nCN yl)propyl]-4-piperidinyl]ethyl]-2-methoxyphenoxy]ethoxy]ethyl ] thio]-2,5-dioxo-1-pyrrolidinyl]ethyl]- $\omega$ -[[7-hydroxy-7-oxido-2,13-dioxo-10-[(1-oxooctadecyl)oxy]-6,8,12-trioxa-3-aza-7phosphatriacont-1-y1]oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

PAGE 1-C

PAGE 1-D

\_\_ (CH2)16-Me

IT 791821-42-6

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of piperidinealkanoic acids as cell targeting compds."
 with selective affinity to ανβ3, ανβ5, or
 ανβ6 integrin receptors for use with imaging agents or
 liposomes)

RN 791821-42-6 HCAPLUS

CN Poly(oxy=1,2-ethanediyl),  $\alpha-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]-\omega-[[7-hydroxy-7-oxido-2,13-dioxo-10-[(1-yl)ethyl]-\delta-[(1-yl)ethyl]-\del$ 

PAGE 1-A:

$$\begin{array}{c|c} CH_2 - CH_2 \\ \hline O - CH_2 - C$$

PAGE 1-F

IT 2055-46-1, 3,4,5,6-Tetrahydro-2-pyrimidinethiol
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant; preparation of piperidinealkanoic acids as cell targeting compds. with selective affinity to ανβ3,
 ανβ5, or ανβ6 integrin receptors for use
 with imaging agents or liposomes)
RN 2055-46-1 HCAPLUS
CN 2(1H)-Pyrimidinethione, tetrahydro- (CA INDEX NAME)



IC ICM A61K031-454 ICS C07D041-02

INCL 514326000; 546207000; 546227000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 6

IT Biological transport

(intracellular; preparation of piperidinealkanoic acids as cell targeting compds. with selective affinity to  $\alpha v \beta 3$ ,

 $\alpha\nu\beta5$  , or  $\alpha\nu\beta6$  integrin receptors for use

with imaging agents or liposomes)

IT 669076-37-3P 791821-34-6P 791821-35-7P 791821-41-5P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of piperidinealkanoic acids as cell targeting compds:

with selective affinity to  $\alpha v \beta 3$ ,  $\alpha v \beta 5$ , or

 $\alpha \nu \beta 6$  integrin receptors for use with imaging agents or liposomes)

TT 669074-85-5P 669074-97-9P 669075-00-7P 669075-01-8P 669075-02-9P 669075-03-0P 669075-04-1P 669075-10-9P 669075-11-0P 669075-12-1P 669075-17-6P 669075-19-8P 669075-21-2P 669075-22-3P 669075-24-5P 669075-27-8P

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669075-30-3P
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669075-28-9P
                669075-29-0P
                               669075-41-6P
                                              669075-48-3P
                669075-39-2P
669075-38-1P
                               669075-51-8P
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669075-49-4P
                669075-50-7P
                               669075-55-2P
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669075-53-0P
                669075-54-1P
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669075-57-4P
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669075-61-0P.
669075-66-5P ""
                669075-67-6P
                               669075-68-7P
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                               669075-81-4P
                                              669075-83-6P
669075-71-2P
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669075-84-7P
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669076-06-6P
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669076-15-7P
                669076-16-8P
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669076-38-4P
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669076-86-2P
791820-71-8P
               791820-74-1P
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791820-93-4P 791820-94-5P
                               791821-24-4P 791821-38-0P
 791821-09-5P
                791821-22-2P
791821-43-7P 791821-44-8P
                               791821-45-9P
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 792931-35-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
    (preparation of piperidinealkanoic acids as cell targeting compds.
    with selective affinity to ανβ3, ανβ5, or
   \alpha v\beta 6 integrin receptors for use with imaging agents or
    liposomes)
75-65-0, 'tert-Butanol, reactions | 99-05-8, 3-Aminobenzoic acid | |
 112-26-5, 1,2-Bis(2-chloroethoxy)ethane 127-08-2, Potassium
 acetate 504-29-0, 2-Aminopyridine
                                       622-26-4, 4-(2-
                           626-55-1, 3-Bromopyridine
                                                       927-58-2,
 Hydroxyethyl)piperidine
 4-Bromobutyryl chloride
                           1066-54-2, Trimethylsilylacetylene
 2635-13-4, 3,4-Methylenedioxyphenyl bromide
                                              5414-19-7,
                           37517-81-0, Methyl 3-chloro-3-
 Bis(2-bromoethyl) ether
 oxopropionate 84358-13-4, 1-tert-Butoxycarbonylpiperidine-4-
                                               658712-81-3
 carboxylic acid 157688-46-5
                                 332884-21-6
 669075-32-5 ... 669076-66-8
                            791821-31-3 791821-42-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
    (preparation of piperidinealkanoic acids as cell targeting compds.
    with selective affinity to \alpha v\beta 3, \alpha v\beta 5, or
    ανβ6 integrin receptors for use with imaging agents or
   liposomés) .
                                      75-15-0, Carbon disulfide,
 74-88-4, Methyl iodide, reactions
                                           580-13-2,
 reactions 98-80-6, Phenylboronic acid
                                                  616-29-5, and the Market
 2-Bromonaphthalene
                     591-19-5, 3-Bromoaniline
                                1073-06-9, 1-Bromo-3-fluorobenzene
 1,3-Diamino-2-hydroxypropane
                                                     1435-52-5, 13 1-1
 1099-45-2, Carbethoxymethylenetriphenylphosphorane
1,4-Dibromo-2-fluorobenzene 1664-54-6, 3-(3-Aminophenyl)propionic
 acid 2055-46-1, 3,4,5,6-Tetrahydro-2-pyrimidinethiol
 2537-48-6, Diethyl cyanomethylphosphonate
                                              5332-24-1,
3-Bromoquinoline 5927-18-4, Trimethyl phosphonoacetate
 6457-49-4, 4-Piperidinemethanol
                                   6638-79-5, N,O-
 Dimethylhydroxylamine hydrochloride
                                       7368-78-7,
                           14338-36-4, 3-Aminophenylacetic acid
 4-Bromo-2-methoxyphenol
 18997-19-8, Chloromethyl pivalate
                                     24424-99-5, Di-tert-butyl
 dicarbonate 76513-69-4, [2-(Trimethylsilyl)ethoxy]methyl chloride
 154775-43-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
   (reactant; preparation of piperidinealkanoic acids as cell targeting
    compds. with selective affinity to \alpha v \beta 3,
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IT

42

 $\alpha\nu\beta5$ , or  $\alpha\nu\beta6$  integrin receptors for use with imaging agents or liposomes)

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ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                      2004:964698 HCAPLUS Full-text
DOCUMENT NUMBER:
                     141:391534
                      Three-dimensional solid phase extraction
TITLE:
                    surfaces
             Gjerde, Douglas T.; Hanna, Christopher T.;
                      Nguyen, Liem; Yengoyan, Leon S.
                                                     Same and the same of the same of the
PATENT ASSIGNEE (S):
                      USA
SOURCE:
                      U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of
                      U.S. Ser. No. 434,713.
                      CODEN: USXXCO
DOCUMENT TYPE:
                      Patent
                      English
LANGUAGE:
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:
  PATENT NO.
                                       APPLICATION NO.
                  KIND
                            DATE
                       A1
                            20041111
                                       US 2004-754775
    US 2004224329
           US 2004126890.
                                       US 2003-434713
                            20040701
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    US 2004224362 A1
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                                       US 2004-792975
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    US 7122640
    WO 2004100887
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                            20041125
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    WO 2004100887 A3 20050519
     W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
        CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
           GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
           KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
           MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,
           SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
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                                      WO 2004-US14458
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            SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
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## 11/091,024

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VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
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PRIORITY APPLN. INFO.:
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                                                  US 2004-792975
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US 2005-658553P

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The subject invention provides extraction capillaries, wherein a substantial portion of the channel is coated with a 3-dimensional solid phase extraction surface that binds an analyte. In some embodiments the extraction matrix comprises a polymer backbone with an extraction agent bound thereto. Analytes of particular relevance include biomols., such as proteins, polynucleotides, lipids and polysaccharides. The invention further provides devices comprising the extraction capillaries, reagents for use in conjunction with the capillaries and devices, and methods for the production and use of the capillaries and devices.

IT 759435-93-3P 790661-49-3P

759435-93-3P 790661-49-3P
RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation) (three-dimensional solid phase extraction surfaces)

RN 759435-93-3 HCAPLUS

CN L-Lysine, N2, N2-bis(carboxymethyl)-N6-(mercaptoacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 790661-49-3 HCAPLUS

CN Dextran, 2-[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]amino]-2-oxoethyl ether, (9CI) (CA INDEX NAME)

CM ...1

CRN 790661-48-2 CMF C8 H10 N2 O4

СМ

CRN 9004-54-0 CMF Unspecified CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*
IC ICM C12Q001-68

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ICS C12M001-34
INCL 435006000; 435287200
CC 9-9 (Biochemical Methods)
     77-77-0DP; Divinyl sulfone, reaction products with dextran
     9004-54-0DP, Dextran, reaction products with divinyl sulfone
                 13822-56-5P 759435-93-3P 790661-49-3P
     RL: ARU (Analytical role, unclassified); SPN (Synthetic
     preparation); ANST (Analytical study); PREP (Preparation)
        (three-dimensional solid phase extraction surfaces)
L32 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                         2004:589589 HCAPLUS Full-text
DOCUMENT NUMBER:
                         141:140952
                         Maleamic acid polymer derivatives and their
                         succinamic acid polymer bioconjugates
                         Kozlowski, Antoni; Gross, Remy F., III; McManus,
INVENTOR(S):
                         Samuel P.
                         Nektar Therapeutics Al, Corporation, USA
PATENT ASSIGNEE(S):
                   Nektar Therapeutics Al, PCT Int. Appl., 71 pp.
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GB, GD, GE,						
KR, KZ, LC,	LK, LR	, LS, LT,	LU, LV, MA,	MD, MG,	MK,	MN, MW,
			PH, PL, PT,			
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VN, YU, ZA,				•		
RW: BW, GH, GM,		,				
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		, BJ, CF,	CG, CI, CM,	GA, GN,	GQ,	GW, ML,
MR, NE, SN,						
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与感觉操作。这是 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, CN 1732207 $(x) = \frac{4^{1/3}}{2^{1/3}}$ ... 20060208 CN 2003-80108082 200312 31 JP 2006522167 20060928 JP 2005-508648 200312 IN 2005DN02712 Α 20070420 IN 2005-DN2712 200506 20 <--PRIORITY APPLN. INFO.: US 2002-437251P 200212  $f_{n} = f(n) + \frac{1}{2}$ US 2003-468340P 200305 05

WO 2003-US41705 W 200312

AB Michael-type addition reaction conjugates of maleimide derivs. of water-soluble polymers are subjected to conditions to open the succinimide ring to give succinamic acid polymer conjugates with improved resistance to hydrolysis and stability during storage.

IT 725274-00-0

RL: PRP (Properties)

Michigan Carlo

(hydrolysis properties of Michael-type addition reaction-prepared products of N-bonded polyethylene glycol derivs. of maleimide)

RN 725274-00-0 HCAPLUS

CN Poly(oxy=1,2-ethanediyl),  $\alpha-[2-[[4-[3-[(2-hydroxyethyl)thio]-2,5-dioxo-1-pyrrolidinyl]methyl]cyclohexyl]carbonyl]amino]ethyl]-<math>\omega$ -methoxy-(9CI) (CA INDEX NAME)

$$\begin{array}{c} O \\ C - NH - CH_2 - CH_2 - \begin{bmatrix} - O - CH_2 - CH_2 \end{bmatrix} & OMe \\ CH_2 \\ O - CH_2 - CH_2$$

illia Presi

725273-96-1D, reaction products with proteins
RL: PRP (Properties)
(hydrolysis rates of Michael-type addition reaction-prepared protein)

conjugates of N-bonded polyethylene glycol derivs. of maleimide)

RN 725273-96-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[3-[[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethyl]amino]-3-oxopropyl]- $\omega$ -methoxy- (9CI) (CA INDEX NAME)

PAGE 1-E

 $-CH_2$  OMe

IT 322725-90-6 724722-27-4

RL: PRP (Properties)

(hydrolysis rates of N-bonded polyethylene glycol derivs. of maleimide)

RN 322725-90-6 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α,α'-[[(1S)-1-[[[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethyl]amino]carb onyl]-1,5-pentanediyl]bis(iminocarbonyl)]bis[ω-methoxy- (CA INDEX NAME)

PAGE 1-B

 $-CH_2$  OMe OCH2  $-CH_2$  OMe

RN

The state of the state of

CN Poly( $oxy=1,2\pi$ ethanediyl),  $\alpha=[2-[[4-[(2,5-dihydro-2,5-dioxo-1]+$ pyrrol-1-yl)methyl]cyclohexyl]carbonyl]amino]ethyl]-w-methoxy-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ \hline & &$$

60-24-2, 2-Mercaptoethanol

RL: RCT (Reactant); RACT (Reactant or reagent) (precursor; manufacture and hydrolysis properties of Michael-type addition reaction-prepared products of N-bonded polyethylene glycol. derivs. of maleimide)

60-24-2 HCAPLUS RN

Ethanol, 2-mercapto- (CA INDEX NAME) CN

но — Сн 2 — Сн 2 — \$ Н

ICM C08G065-00 IC '

35-8 (Chemistry of Synthetic High Polymers) Section cross-reference(s): 6, 34

724722-33-2 724722+36-5 725274-00-0 IT

RL: PRP (Properties)

(hydrolysis properties of Michael-type addition reaction-prepared products of N-bonded polyethylene glycol derivs. of maleimide)

99126-64-4D, reaction products with proteins 725273-96-1D, IT

reaction products with proteins

RL: PRP (Properties)

(hydrolysis rates of Michael-type addition reaction-prepared protein conjugates of N-bonded polyethylene glycol derivs. of maleimide)

99126-64-4 322725-90-6 724722-27-4 724722-92-3 ΙT

725273-90-5 725273-91-6 725273-92-7 724723-02-8

RL: PRP (Properties)

(hydrolysis rates of N-bonded polyethylene glycol derivs. of maleimide)

ΙT 60-24-2, 2-Mercaptoethanol 292170-95-7

RL: RCT (Reactant); RACT (Reactant or reagent) (precursor; manufacture and hydrolysis properties of Michael-type addition reaction-prepared products of N-bonded polyethylene glycol 21 4 derivs. of maleimide)

, 3.3 L32 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN 2004:589588 HCAPLUS Full-text ACCESSION NUMBER: 141:140951 DOCUMENT NUMBER:

Hydrolytically stable maleimide-terminated

polymers and their preparation

11/091,024

```
Kozlowski, Antoni; Gross, Remy F., III; McManus,
INVENTOR(S):
                        Samuel P.
PATENT ASSIGNEE(S):
                        Nektar Therapeutics Al, Corporation, USA
                        PCT Int. Appl., 118 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
    PATENT NO. KIND
                                          APPLICATION NO. DATE
                              DATE
                              20040722
                                          WO 2003-US41699
    WO 2004060965
                                                                200312
                                                               31
                              20041007
    WO 2004060965
                         Α3
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
           CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
            GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
            SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
       VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
           AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
          DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
           SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
            MR; NE, SN, TD, TG
               A1
    CA 2509153
                              20040722
                                          CA 2003-2509153
                                                                200312.
            State of the
                                                                31
                               20040729
                                          AU 2003-300133
    AU 2003300133
                                                              200312
                                                               31
    EP 1578842
                                          EP 2003-800391
                               20050928
                         A2
                                                                200312
                                                                31
                                               <--
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
          PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,
           SK
                                          CN 2003-80108010
     CN 1732206
                               20060208
                         A.
                                                                200312
                                          JP 2004-564914
     JP 2006512445
                               20060413
                                                                200312
                                                                31
                                          IN 2005-DN2631
                               20070302
     IN 2005DN02631
                                                               200506
                                          US 2002-437211P
PRIORITY APPLN. INFO .:
                                                               200212
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WO 2003-US41699

20031

GΙ

$$POLY = O = O = O = NH = X = N$$

The hydrolytically stabilized maleimide-functionalized water-soluble polymer I (POLY = water-soluble polymer segment; b = 0, 1; X = a hydrolytically stable linker containing ≥3 contiguous saturated carbon atom) is absent aromatic groups and ester linkages.

and ester linkages.

1T 724721-96-4P 724722-30-9P 724722-47-8P 724722-58-1P 724722-68-3P 724722-77-4P 724722-80-9P 724722-83-2P 724722-86-5P

RL: IMF (Industrial manufacture); PREP (Preparation)
(preparation of hydrolytically stable maleimide-terminated polymers)

RN 724721-96-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α,α'-[[(1S)-1-[[[2-[[7-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxoheptyl]amino]ethyl]amino]carb onyl]-1,5-pentanediyl]bis(iminocarbonyl)]bis[ω-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-B

$$-CH_2$$
 OMe

RN 724722-30-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[15-[3-[(2-hydroxyethyl)thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxo-6,9,12-trioxa-2-azapentadec-1-yl]-

ω-methoxy (9CI) (CA INDEX NAME)

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PAGE 1-A

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·福德哲学/图图图像 (1995)

a vista da galama fin tip 🕻

PAGE 1-B

$$-CH_2$$
 OMe

RN 724722-47-8 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[3-[[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]methyl]amino]-3-oxopropyl]-ω-methoxy- (9CI) (CA INDEX NAME)

$$MeO = \begin{bmatrix} CH_2 - CH_2 -$$

RN 724722-58-1 HCAPLUS

医克里氏试验检检验 医抗

CN Poly(oxy=1,2-ethanediyl), α-[3-[[(trans)-4-(2,5-dihydro=2,5-dioxo-1H-pyrrol=1-yl)cyclohexyl]methyl]amino]-3-oxopropyl]-ω-methoxy-(9CI) (CA INDEX NAME)

MeO 
$$\begin{bmatrix} CH2-CH2-O \\ n \end{bmatrix}$$
  $CH2-CH2-C-NH-CH2$ 

RN 724722-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[3-[[(trans)-4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)cyclohexyl]amino]-3-oxopropyl]-ω-methoxy (9CI) (CA INDEX NAME)

MeO 
$$CH2-CH2+O$$
  $n$   $CH2-CH2-C-NH$ 

RN 724722-77-4 HCAPLUS.

医骶线 阿弗雷斯克克克克斯

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[3-[[4-[[3-[(2-hydroxyethyl)thio]-2,5-dioxo-1-pyrrolidinyl]methyl]cyclohexyl]methyl]amino]-3-oxopropyl]-<math>\omega$ -methoxy- (9CI) (CA INDEX NAME)

RN 724722-80-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[3-[[(trans)-4-[3-[(2-hydroxyethyl)thio]-2,5-dioxo-1-pyrrolidinyl]cyclohexyl]methyl]amino]-3-oxopropyl]- $\omega$ -methoxy- (9CI) (CA INDEX NAME)

MeO 
$$CH2-CH2-O$$
  $CH2-CH2-CH2-CH2-CH2$ 

S= $CH2-CH2-OH$ 

CN Poly(oxy=1,2-ethanediy1), α-[3-[(trans)-4-[3-[(2-hydroxyethy1)thio]-2,5-dioxo-1-pyrrolidiny1]cyclohexy1]amino]-3-oxopropy1]-ω-methoxy- (9CI) (CA INDEX NAME)

MeO 
$$\begin{bmatrix} \dot{c}H\dot{2}-CH_2-O \\ \end{bmatrix}_n$$
  $CH_2-CH_2-C-NH$   $CH_2-CH_2-CH_2-CH_2-OH$ 

RN +724722-86-5 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[3-[[3-[(2-hydroxyethyl)thio]-2,5-dioxo-1-pyrrolidinyl]methyl]cyclohexyl]methyl]amino]-3-oxopropyl]-ω-methoxy- (9CI) (CA INDEX NAME)

IT 724723-05-1DP, mercapto protein derivs.

RL: IMF (Industrial manufacture); PRP (Properties); PREP

(Preparation)

(preparation of hydrolytically stable maleimide-terminated polymers)

RN 724723-05-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[[[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethyl]amino]carbonyl]-<math>\omega$ -methoxy-(9CI) (CA INDEX NAME)

IT 724722-20-7P 724722-27-4P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP

11/091,024

54

(Preparation); RACT (Reactant or reagent)

Transference State

(preparation of hydrolytically stable maleimide-terminated polymers)

RN 724722-20-7 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[15-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxo-6,9,12-trioxa-2-azapentadec-1-yl]- $\omega$ -methoxy-(9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-1

$$-CH_2 - n$$
 OMe

RN 724722-27-4 HCAPLUS

CN Poly(oxy=1,2-ethanediyl),  $\alpha-[2-[[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]carbonyl]amino]ethyl]-<math>\omega$ -methoxy-(9CI)- (CA\_INDEX\_NAME)

$$\begin{array}{c|c} O \\ C - NH - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - OMe \\ \hline \\ CH_2 \\ O - N - O \end{array}$$

IT 724722-38-7

RL: PRP (Properties)

(preparation of hydrolytically stable maleimide-terminated polymers)

RN 724722-38-7 HCAPLUS

CN Poly(oxy-1,2-ethanediy1),  $\alpha$ -[2-[[[4-[3-[(2-hydroxyethy1)thio]-2,5-dioxo-1-pyrrolidiny1]cyclohexy1]acety1]amino]ethy1]- $\omega$ -methoxy- (9CI) (CA INDEX NAME)

 $(a_{k,k_{k}}^{(k)}, b_{k}^{(k)}) = 0 \quad \forall \quad k \in \mathbb{N}^{k}$ 

MeO 
$$CH_2 + CH_2 - O$$
  $n$   $CH_2 - CH_2 - NH - C - CH_2$ 

O  $N$   $O$   $S - CH_2 - CH_2 - OH$ 

IT 724722-75-2

RL: TEM (Technical or engineered material use); USES (Uses)
(preparation of hydrolytically stable maleimide-terminated polymers)

RN 724722-75-2 HCAPLUS

三海 医克特雷氏试验检

CN Poly(exy-1,2-ethanediyl),  $\alpha-[3-[[[3-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]methyl]amino]-3-oxopropyl]-<math>\omega$ -methoxy- (9CI) (CA INDEX NAME)

MeO 
$$CH_2$$
  $CH_2$   $O$   $CH_2$   $O$   $O$ 

IT 60-24-2, 2-Mercaptoethanol
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (starting material; preparation of hydrolytically stable
 maleimide-terminated polymers)

RN 60-24-2 HCAPLUS

CN Ethanol, 2-mercapto- (CA INDEX NAME)

HO-CH2-CH2-SH

IC ICM C08G065-00

CC 35-8 (Chemistry of Synthetic High Polymers)

RL: IMF (Industrial manufacture); PREP (Preparation)

(preparation of hydrolytically stable maleimide-terminated polymers)

99126-64-4DP, mercapto protein derivs. 724723-05-1DP, mercapto protein derivs.

RL: IMF (Industrial manufacture); PRP (Properties); PREP (Preparation)

网络美国大学

US 2004037802

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US 2002-218167

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(preparation of hydrolytically stable maleimide-terminated polymers)
     664348-92-9P 664350-10-1P
IT
                                  724722-10-5P
                                                 724722-17-2P
     724722-20-7P 724722-27-4P
                                724722-44-5P
     724722-53-6P 724722-56-9P
                                  724722-63-8P
                                                 724722-65-0P
     724722-72-9P
    RL: IMF (Industrial manufacture); RCT (Reactant); PREP
     (Preparation); RACT (Reactant or reagent)
       (preparation of hydrolytically stable maleimide-terminated polymers)
IT
     99126-64-4 724722-33-2
                               724722-36-5 724722-38-7
     724722 - 89 - 8 - 724722 - 92 - 3
                               724723-02-8
                                                                与指令人的第二人
    RL: PRP (Properties)
        (preparation of hydrolytically stable maleimide-terminated polymers)
    724722-75-2
IT
    RL: TEM (Technical or engineered material use); USES (Uses)
       (preparation of hydrolytically stable maleimide-terminated polymers)
     60-24-2, 2-Mercaptoethanol 76-05-1, Trifluoroacetic acid,
IT
                107-15-3, 1,2-Ethanediamine, reactions
                                                         110-52-1
    reactions
     629-03-8 2549-93-1, 1,4-Cyclohexane(bismethylamine)
                                                           2579-20-6,
                                               9004-74-4
     1,3-Cyclohexanedimethanamine
                                   4246-51-9
                                                           55750-48-6
    64987-85-5 80506-64-5
                               159540-80-4 177583-27-6 266313#9545 EREPORT
    724721-93-1
                  724722-41-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (starting material; preparation of hydrolytically stable
        maleimide-terminated polymers)
             Programme State of the
    ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
                         2004:142994 HCAPLUS Full-text
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         140:205131
                        Releasable polymeric conjugates based on
                        aliphatic biodegradable linkers
INVENTOR(S):
                         Zhao, Hong; Greenwald, Richard B.; Pendri,
                        Annapurna
PATENT ASSIGNEE(S):
                        Enzon, Inc., USA
         一次 植感染色色 医毛囊
                        PCT Int. Appl., 85 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                                            APPLICATION NO.
     PATENT NO.
                         KIND
                                DATE
     WO 2004014424
                                                            建工程 化电影 化电影 医二氏管 医二氏管
                                20040219
                                           WO 2003-US25252
                                                                 200308
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, Se
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
             NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA,
             ZM, ZW
      RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
            SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
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200208
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    US 7122189
                            20061017
                      B2
    CA 2493329
                      A1
                            20040219
                                      CA 2003-2493329
                                                          200308
                                                           13
    AU 2003262622
                                                        海海 化多电路 萨尔特人特
                            20040225
                                      AU 2003-262622
                      A1
                                                         :200308
    EP 1534334
                            20050601
                                      EP 2003-785231
                                                         200308
                                                          13
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
           PT, TE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, BE
           SK
    JP 2006505634
                            20060216
                                      JP 2004-528078
                                                          200308
       US 2006286065
                                      US 2006-502108
                            20061221
                      Α1
                                                          200608
                                                           09
                                      US 2002-218167
PRIORITY APPLN. INFO .:
                                                         200208
                                                          13
                                      WO 2003-US25252
                                                          200308
                                                          .13
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OTHER SOURCE(S): MARPAT 140:205131

4. 作用意思的表示。

AB Activated polymeric bicine derivs. such as, as well as their conjugates are disclosed. Methods of making and using the bicine derivs. as prodrugs for treatment and diagnosis are also disclosed. For example, doxorubicin and daunorubicin prodrugs containing a polyethylene glycol derivative were prepared IT 96-53-7, 2-Mercaptothiazoline

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polymeric conjugates based on aliphatic biodegradable linkers as prodrugs)

RN 96-53-7 HCAPLUS

CN 2-Thiazolidinethione (CA INDEX NAME)

S s

IT 660843-24-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL
(Biological study); PREP (Preparation); USES (Uses)
(preparation of polymeric conjugates based on aliphatic biodegradable linkers as prodrugs)

RN 660843-24-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha,\alpha'-[14-[2-[2-[2-[2-(2,5$ dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethoxy]ethoxy]ethyl]amino]-2oxoethyl]-1,10,18,27-tetraoxo-5,8,11,17,20,23-hexaoxa-2,14,26triazaheptacosane+1,27-diyl|bis[ω-methoxy- (9CI) (CA INDEX

PAGE 1-A CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-NH-C-CH2-N-CH2-CH2-CH2-

$$-CH_{2}-O-CH_{2}-CH_{2}-O-CH_{2}-CH_{2}-NH-C-CH_{2}-NH-C-CH_{2}-CH_{2}-CH_{2}-NH-C-CH_{2}-CH_{2}-CH_{2}-CH_{2}-NH-C-CH_{2}-CH_{2}-CH_{2}-CH_{2}-NH-C-CH_{2}-CH_{2}-CH_{2}-CH_{2}-NH-C-CH_{2}-$$

IC ICM A61K039-395 CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 33, 35

96-53-7, 2-Mercaptothiazoline 111-42-2, reactions IT 929-06-6, 2-(2-Aminoethoxy)-ethanol 1142-20-7 5292-43-3 5893-05-0, N-Trityl glycine 23541-50-6, Daunorubicin hydrochloride: 25316-40-9, Doxorubicin hydrochloride 39927-08-7 tert-Butyl-N-(3-hydroxypropyl)-carbamate 74124-79-1, 124661-64-9 135649-01-3 N, N'-Disuccinimidyl carbonate 204133-37-9 660843-10-7 153086-78-3 172502-50-0 RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of polymeric conjugates based on aliphatic biodegradable linkers as prodrugs)

660843-09-4P 660842-98-8P 660441-02-1P 660441-08-7P 660843-36-7P 660843-19-6P 660843-24-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of polymeric conjugates based on aliphatic biodegradable

linkers as prodrugs)

THERE ARE 4 CITED REFERENCES AVAILABLE FOR REFERENCE COUNT: THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN 2003:963137 HCAPLUS Full-text ACCESSION NUMBER: DOCUMENT NUMBER: 141:191083

Synthesis and characterization of new optically TITLE: active monomers containing imide rings Cianga, Luminita; Popescu, Florin

AUTHOR(S):

11/091,024

CORPORATE SOURCE:

"Petru Poni" Institute of Macromolecular

Chemistry, Iasi, R-6600, Rom.

SOURCE:

Buletinul Stiintific al Universitatii

"Politehnica" din Timisoara Romania, Seria

Chimie si Mediului (1999), 44(2),

125-132

CODEN: BSIMFG; ISSN: 1224-6018

Universitatii "Politehnica" din Timisoara PUBLISHER:

DOCUMENT TYPE:

Journal

LANGUAGE:

English

Two optically active diols with imide rings were synthesized from aromatic AB dianhydride and (R)-2-amino-1-butanol (AMB). Secondary products with zwitterionic structure were obtained concomitantly with diacetylated ones in the case of chemical imidization reaction at low temperature A reaction mechanism between dianhydride and AMB was proposed, too. Optically active bismaleimide and Nphenylmaleimide type monomers were synthesized starting from 4-maleimidobenzoic acid or its acid chloride. Some optically active polymers containing different type of imide rings were obtained by polyaddn. reactions from described monomers.

52-90-4, L-Cysteine, reactions IT

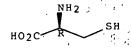
RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis and characterization of optically active diols containing imide rings for polyurethanes and polyimide polythioethers)

52-90-4 HCAPLUS RN

L-Cysteine (CA INDEX NAME)

Absolute stereochemistry.



287488-68-0P 287488-69-1P 740846-73-5P IT

740846-74-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis and characterization of optically active diols containing imide rings for polyurethanes and polyimide polythioethers)

RN 287488-68-0 HCAPLUS

L-Cystine, N.N.-bis[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)benzoyl]-CN

, polymer with 1,5-pentanedithiol (9CI) (CA INDEX NAME)

CM

CRN 287488-62-4

C28 H22 N4 O10 S2 CMF

Absolute stereochemistry. Rotation (-).

医肾髓炎 经通货 

ar project subject (1917)。

JOSEPH (1997年) 1997年

CM 2

CRN 928-98-3 CMF C5 H12 S2

HS-(CH2)5-SH

RN

287488-69-1 HCAPLUS

CN L-Lysine, N2,N6-bis[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)benzoyl], polymer with 1,5-pentanedithiol (9CI) (CA INDEX NAME)

CM

CRN 287488-63-5 CMF C28 H24 N4 O8

Absolute stereochemistry.

CM 2

CRN 928÷98÷3 CMF C5 H12 S2

HS-(CH2)5-SH.

RN 740846-73-5 HCAPLUS

CN Benzoic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-y1)-,

(2R)-2-[[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-y1)benzoyl]amino]butyl
ester, polymer with 1,5-pentanedithiol (9CI) (CA INDEX NAME)

CM: 1

CRN 287488-65-7 CMF C26 H21 N3 O7

Absolute stereochemistry. Rotation (-).

CM 2

CRN 928-98-3 CMF C5 H12 S2

HS-(CH2)5-SH

RN 740846-74-6 HCAPLUS

CN Poly[(2,5-dioxo-1,3-pyrrolidinediyl)thio-1,5-pentanediylthio(2,5-dioxo-3,1-pyrrolidinediyl)-1,4-phenylenecarbonylimino[(1R)-1-carboxy-1,2-ethanediyl]dithio[(2R)-2-carboxy-1,2-ethanediyl]iminocarbonyl-1,4-phenylene] (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CC 35-2 (Chemistry of Synthetic High Polymers)

IT 52-90-4, L-Cysteine, reactions 56-45-1, L-Serine, reactions 56-87-1, L-Lysine, reactions 89-32-7, Pyromellitic dianhydride 464-45-9 2421-28-5, Benzophenonetetracarboxylic acid dianhydride 5856-63-3, (R)-2-Amino-1-butanol 17057-04-4, 4-Maleimidobenzoic acid 29305-46-2, 4-Maleimidobenzoic acid chloride

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis and characterization of optically active diols containing imide rings for polyurethanes and polyimide polythioethers)

TT 287488-62-4P 287488-63-5P 287488-64-6P 287488-65-7P

287488-66-8P 287488-68-0P 287488-69-1P

740846-69-9P 740846-70-2P 740846-71-3P 740846-72-4P

740846-73-5P 740846-74-6P

化氯甲基甲基苯基

RL: SPN (Synthetic preparation); PREP (Preparation)

```
(synthesis and characterization of optically active diols containing
imide rings for polyurethanes and polyimide polythioethers)
                   20
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REFERENCE COUNT:

THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:454093 HCAPLUS Full-text DOCUMENT NUMBER: 139:26651

Modified lipids as delivery vehicles for

therapeutic agents

INVENTOR(S): Jorgensen, Michael; Keller, Michael; Miller,

Andrew David; Perouzel, Eric

PATENT ASSIGNEE(S): Mitsubishi Chemical Corporation, Japan

PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KIN	IND DATE		· ;	APPLICATION NO.			DATE			
WO 2003047549	A2	20030	0612	Ţ	, NO 2	002-	GB54	71	i 1,	20	00212
						_	•			. 04	4
WO 2003047549;	А3	2003	2.31			<				1 .	
W: AE, AG, AL,				BA.	BB.	BG.	BR.	BY.	B7.	CA.	CH.
CN, CO, CR,											
GE, GH, GM,	HR,	HU, ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	KZ,
LC, LK, LR,											
NO, NZ, OM,											
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PT, IE, SI,										1 1 3 1	

JP 2005515990 20050602

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US 2005064023 A1

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A1 20050324

US 2004-496970

200410 22

海点工作 电流流管

PRIORITY APPLN. INFO.:

GB 2001-29121

200112

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<--WO 2002-GB5471

200212

OTHER SOURCE(S):

MARPAT 139:26651

The present invention provides a delivery vehicle for a therapeutic agent comprising a modified lipid and a therapeutic agent (e.g., DNA); wherein the modified lipid comprises a lipid and a delivery, targeting or stabilizing moiety (DTS moiety); wherein the lipid is linked to the DTS moiety via a linker which is stable in biol. fluid and which is unstable in defined conditions; and wherein the DTS moiety is linked to the lipid alter formation of a complex of lipid and therapeutic agent. Thus, a cholesterol-containing lipid was obtained by the reaction of a cholesterol derivative with a serine derivative Liposomes were obtained from DOPE and the above lipid. The addition of PEG dialdehyde stabilized the liposomes.

IT 539792-14-8P 539792-18-2P 539792-21-7P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (in preparation of PEG-lipid systems; modified lipids as delivery vehicles for therapeutic agents)

RN 539792-14-8 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)butyl]-\omega-[4-[[2-[[(2Z)-3-carboxy-1,5-dioxo-5-(pentafluorophenoxy)-2-pentenyl]amino]ethyl]amino]-4-oxobutoxy]-(9CI) (CA INDEX NAME)$ 

PAGE 1-A

PAGE 1-B

$$-C - CH = C - CH_2 - C - O$$

$$F$$

$$F$$

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RN 539792-18-2 HCAPLUS

医内侧性神经病 的复数形式

CN Cholest-5-en-3-ol  $(3\beta)$ -, [2-[[(2R)-2-amino-3-mercapto-1-oxopropyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

-CHMe2

RN 539792-21-7 HCAPLUS

(4) 사람 (1) (4)

CN Cholest-5-en-3-ol  $(3\beta)$ -, [2-[[3-[[(2R)-2-amino-3-mercapto-1-oxopropyl]amino]propyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

- (CH2)3 CHMe2

IT 539792-11-5P 539792-12-6P 539792-13-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(in preparation of PEG-lipid systems; modified lipids as delivery vehicles for therapeutic agents)

RN 539792-11-5 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)butyl]-\omega-[4-[(2,2-dimethoxyethyl)amino]-4-oxobutoxy]- (9CI) (CA INDEX NAME)$ 

RN 539792-12-6 HCAPLUS

[1] 李紫芷,夏凉芷

CN Poly(oxy-1,2-ethanediy1),  $\alpha-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-y1)buty1]-\omega-[4-[(2-oxoethy1)amino]-4-oxobutoxy]-(9CI) (CA INDEX NAME)$ 

$$(CH2)4$$
  $O-CH2-CH2$   $O-CH2-CH2$   $O-CH2-CH2$   $O-CH2-CH2$   $O-CH2-CH2-CH2$ 

RN 539792-13-7 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[4-[(2-aminoethyl)amino]-4-oxobutyl]-\omega-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)butoxy]-(9CI) (CA INDEX NAME)$ 

IC ICM A61K009-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 32, 34

IT Polyoxyalkylenes, biological studies
RI: PEP (Physical engineering or che)

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(dialdehyde derivative; modified lipids as delivery vehicles for therapeutic agents)

IT Polyoxyalkylenes, biological studies

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(modified lipids as delivery vehicles for therapeutic agents)

IT DNA

Lipids, biological studies Nucleotides, biological studies

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11/091,024
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (modified lipids as delivery vehicles for therapeutic agents)
IT
     539792-18-2P 539792-19-3P
                                 539792-20-6P
     539792-21-7P
                   539792-22-8P
                                 539792-23-9P
    RL: PEP (Physical, engineering or chemical process); PYP (Physical
    process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
       (in preparation of PEG-lipid systems; modified lipids as delivery
       vehicles for therapeutic agents)
IT
     105069-83-8P 123628-75-1P
                                                284494-09-3P
                                 136099-11-1P
    436147-53-4P 436147-54-5P
                                 436147-55-6P
                                                436147-56-7P
     437712-87-3P 437712-88-4P 539792-11-5P
     539792-12-6P 539792-13-7P
                               539792-15-9P
    539792-24-0P
                   539792-25-1P
                                 539792-26-2P
                                                539792-27-3P
    539792-28-4P
                   539792-31-9P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
    RACT (Reactant or reagent)
       (in preparation of PEG-lipid systems; modified lipids as delivery
       vehicles for therapeutic agents)
L32 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                        2003:129325 HCAPLUS Full-text
DOCUMENT NUMBER:
                        138:193258
TITLE:
                        Methods of imaging and treatment with targeted
                        compositions
INVENTOR(S):
                        Unger, Evan C.; Wu, Yungiu
PATENT ASSIGNEE(S):
                        Bristol-Myers Squibb Medical Imaging, Inc., USA
SOURCE:
                        U.S., 96 pp., Cont.-in-part of U.S. Ser. No.
                        218,660.
                        CODEN: USXXAM
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6521211	B1	20030218	US 1999-243640	
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CN 1187137	Α	19980708	CN 1996-194499	1:
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CN 1083280 EP 1444991	B Al	20020424 20040811	EP 2004-76279	The second of the section
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R: AT, BE, CH, PT, IE, FI	DE, DK	, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC,
CA 2362200 Charles	A1	20000810	CA 2000-2362200	200002
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WO 2000045856 =
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                                     20010215
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              CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
               LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,
               SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN,
               YU, ZA, ZW.
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
               DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1146911
                             A2 20011024
                                               EP 2000-914480
                                                                           1 200002
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
                      B2; 20041007
     AU 777304
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     US 2003157025
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                                                 US 2003-341167
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PRIORITY APPLN. INFO.:
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                                                  WO 2000-US2620
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The invention concerns novel ultrasound methods comprising administering to a patient a targeted vesicle composition which comprises vesicles comprising a AΒ lipid, protein or polymer, encapsulating a gas, in combination with a targeting ligand, and scanning the patient using ultrasound. The scanning may comprise exposing the patient to a first type of ultrasound energy and then interrogating the patient using a second type of ultrasound energy. The targeting ligand preferably targets tissues, cells or receptors, including myocardial cells, endothelial cells, epithelial cells, tumor cells and the glycoprotein GPIIbIIIa receptor. The methods may be used to detect a thrombus, enhancement of an old or echogenic thrombus, low concns. of vesicles and vesicles targeted to tissues, cells or receptors.

186750-26-5P 497861-52-6P 497861-53-7DP, ΙT conjugate with protein A

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(methods of imaging and treatment with targeted compns.)

186750-26-5 HCAPLUS RN

Poly(oxy-1,2-ethanediyl),  $\alpha$ -[2-[[3-(2,5-dihydro-2,5-dioxo-1H-CN  $pyrrol-1-yl)-1-oxopropyl] amino] ethyl]-\omega-[[(15R)-12-hydroxy-12$ oxido-4,7,18-trioxo-15-[(1-oxohexadecyl)oxy]-11,13,17-trioxa-3,8diaza-12-phosphatritriacont-1-yl]oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE :1-B

-(CH2)14---Me

497861-52-6 HCAPLUS RN Poly(oxy-1,2-ethanediyl),  $\alpha-[2-[4-(2R)-2,3-bis](1-R)$ CN

 $oxohexadecyl) oxy] propoxy]-1, 4-dioxobutyl] amino] ethyl]-\omega-[2-[[3-dioxobutyl]] amino] amino] ethyl]-\omega-[2-[[3-dioxobutyl]] amino] ethyl] amino] ethyl]-\omega-[2-[[3-dioxobutyl]] amino] ethyl]-\omega-[2-[[3-dioxobutyl]] amino] ethyl] ethyl]-\omega-[2-[[3-dioxobutyl]] amino] ethyl] ethyl]-\omega-[2-[[3-dioxobutyl]] amino] ethyl] ethyl[3-dioxobutyl] ethyl[3-dioxobutyl$ (2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1oxopropyl]hydroxyamino]ethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

$$CH_2-CH_2-CH_2-CH_2-CH_2-O$$
 $CH_2-CH_2-CH_2-CH_2-O$ 
 $CH_2-CH_2-CH_2-CH_2-O$ 

PAGE 1-B

497861-53-7 HCAPLUS RN

Poly(oxy-1,2-ethanediyl),  $\alpha$ -[(15R)-12-hydroxy-12-oxido-4,7,18-CN trioxo-15-[(1-oxohexadecyl)oxy]-11,13,17-trioxa-3,8-diaza-12-, phosphatritriacont-1-y1]- $\omega$ -[2-[[3-(mercaptothio)-1oxopropyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

$$HS - S - CH_2 - CH_2$$

IC

A61R009-127; A61R038-00; A61R038-04

INCL 424009520; 424009510; 424009520; 424009500; 424450000; 600431000; 600437000; 514018000; 514002000

63-6 (Pharmaceuticals) CC

Section cross-reference(s): 14, 37

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186750-28-7P
                    186750-14-1P 186750-26-5P
    186750-11-8P
                                   221553-44-2DP, conjugate with protein
IT
    186750-29-8P 186750-31-2P
                                                      287952-93-6P
                                       287952-92-5P
                        287952-89-0P
         221553-48-6P
                                                  497861-51-5P
                                   497861-50-4P
                  287952-99-2P
     287952-95-8P
     497861-52-6P 497861-53-7DP, conjugate with protein
                        497861-55-9P
     RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
         497861-54-8P
     (Analytical study); PREP (Preparation); USES (Uses)
        (methods of imaging and treatment with targeted compns.)
                               THERE ARE 546 CITED REFERENCES AVAILABLE
REFERENCE COUNT:
                               FOR THIS RECORD. ALL CITATIONS AVAILABLE
                               IN THE RE FORMAT
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HCAPLUS COPYRIGHT 2007 ACS on STN L32 ANSWER 12 OF 25 2002:4992 HCAPLUS Full-text ACCESSION NUMBER: 136:241803 DOCUMENT NUMBER: Membrane-active properties of  $\alpha\text{-MSH}$ analogs: aggregation and fusion of liposomes TITLE: triggered by surface-conjugated peptides Lima de Souza, Debora; Frisch, Benoit; AUTHOR(S): Duportail, Guy; Schuber, Francis Laboratoire de Chimie Bioorganique, Universite Louis Pasteur, Faculte de Pharmacie, UMR 7514 CORPORATE SOURCE: CNRS/ULP, Illkirch, 67400, Fr. Biochimica et Biophysica Acta, Biomembranes ( SOURCE: 2002), 1558(2), 222-237 CODEN: BBBMBS; ISSN: 0005-2736 Elsevier B.V. PUBLISHER: Journal

DOCUMENT TYPE: English Reaction of the melanotropin hormone analogs [Nle4,D-Phe7]- $\alpha$ - MSH and [Nle4,D-LANGUAGE: Phe7]- $\alpha$ -MSH(4-10), which were extended at their N-terminus by a thiol-AΒ

functionalized spacer arm, with preformed liposomes containing thiol-reactive (phospho)lipid derivs. resulted in the aggregation of the vesicles and in a partial leakage of their inner contents. This aggregation/leakage effect, which was only observed when the peptides were covalently conjugated to the surface of the liposomes, was correlated with the fusion of the vesicles as demonstrated by the observed decrease in resonance energy transfer between probes in a membrane lipid mixing assay. A limited fusion was confirmed by monitoring the mixing of the liposome inner contents (formation of 1-aminonaphthalene-3,6,8-trisulfonic acid/p-xylene bis(pyridinium bromide) complex). The membrane-active properties of the peptides could be correlated with changes in the fluorescence emission spectra of their tryptophan residue, which suggested that after their covalent binding to the outer surface of the liposomes they can partition within the core of the bilayers. A blue shift of 10 nm was observed for [Nle4,D-Phe7]- $\alpha$ -MSH which was correlated with an increase in fluorescence anisotropy and with changes in the accessibility of the coupled peptide as assessed by the quenching of fluorescence of its tryptophan residue by iodide (Stern-Volmer plots). These results should be related to the previously described capacity of  $\alpha\textsc{-MSH}$ , and analogs, to interact with membranes and with the favored conformation of these peptides which, via a  $\beta$ turn, segregate their central hydrophobic residues into a domain that could insert into membranes and, as shown here, trigger their destabilization.

RL: BUU (Biological use, unclassified); PEP (Physical, engineering 404354-30-9 or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)

(aggregation and fusion of liposomes triggered by surface-conjugated peptides in membrane-active properties of α-MSH analogs)

RN 404354-30-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]amino]carbonyl]- $\omega$ -[[(9R)-6-hydroxy-6-oxido-1,12-dioxo-9-[(1-oxohexadecyl)oxy]-5,7,11-trioxa-2-aza-6-phosphaheptacos-1-yl]oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

IT 158470-38-3 158470-38-3D, conjugates with
 phospholipid thiol-reactive derivs. 342643-63-4
 342643-63-4D, conjugates with phospholipid thiol-reactive
 derivs.

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)

(aggregation and fusion of liposomes triggered by surface-conjugated peptides in membrane-active properties of  $\alpha\text{-MSH}$  analogs)

RN 158470-38-3 HCAPLUS

CN α1-13-Corticotropin, N-(3-mercapto-1-oxopropyl)-4-L-norleucine-7-D-phenylalanine-13-L-valinamide-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

RN 158470-38-3 HCAPLUS

CN  $\alpha$ 1-13-Corticotropin, N-(3-mercapto-1-oxopropyl)-4-L-norleucine-7-D-phenylalanine-13-L-valinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

RN 342643-63-4 HCAPLUS

CN Glycinamide, N-(3-mercapto-1-oxopropyl)glycyl-L-norleucyl-L- $\alpha$ -glutamyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

RN 342643-63-4 HCAPLUS

CN Glycinamide, N-(3-mercapto-1-oxopropyl)glycyl-L-norleucyl-L- $\alpha$ -

glutamyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry

PAGE 1-B

CC 2-2 (Mammalian Hormones)

Section cross-reference(s): 63

IT Cell membrane

Fusion, biological

Hydrophobicity

Liposomes

Self-association

Sulfhydryl group

β-Turn

(aggregation and fusion of liposomes triggered by

surface-conjugated peptides in membrane-active properties of

 $\alpha$ -MSH analogs)

IT Membrane, biological

(bilayer; aggregation and fusion of liposomes triggered by surface-conjugated peptides in membrane-active properties of

α-MSH analogs)

IT Phosphatidylcholines, biological studies

Phosphatidylglycerols

RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)

(liposomes; aggregation and fusion of liposomes triggered by surface-conjugated peptides in membrane-active properties of

 $\alpha$ -MSH analogs)

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Phospholipids, biological studies
    RL: BUU (Biological use, unclassified); PEP (Physical, engineering,
    or chemical process); BIOL (Biological study); PROC (Process); USES
     (Uses)
        (thiol-reactive derivs.; aggregation and fusion of liposomes
       triggered by surface-conjugated peptides in membrane-active
        properties of \alpha-MSH analogs)
                                             404354-31-0
                  404354-29-6 404354-30-9
    404354-28-5
IΤ
    RL: BUU (Biological use, unclassified); PEP (Physical, engineering
    or chemical process); BIOL (Biological study); PROC (Process); USES:
        (aggregation and fusion of liposomes triggered by
      surface-conjugated peptides in membrane-active properties of
        \alpha-MSH analogs)
     37213-49-3D, \alpha-MSH, analogs 158470-38-3
ΙT
     158470-38-3D, conjugates with phospholipid thiol-reactive
     derivs. 342643-63-4 342643-63-4D, conjugates
     with phospholipid thiol-reactive derivs.
     RL: PEP (Physical, engineering or chemical process); PRP
     (Properties); PROC (Process)
        (aggregation and fusion of liposomes triggered by
        surface-conjugated peptides in membrane-active properties of
        \alpha-MSH analogs)
     57-88-5, Cholesterol, biological studies
                                                185463-23-4,
IT
     RL: BUU (Biological use, unclassified); PEP (Physical, engineering)
     or chemical process); BIOL (Biological study); PROC (Process); USES
     (Uses)
        (liposomes: aggregation and fusion of liposomes triggered by
        surface-conjugated peptides in membrane-active properties of
        \alpha-MSH analogs)
                                THERE ARE 63 CITED REFERENCES AVAILABLE
REFERENCE COUNT:
                          63
                                FOR THIS RECORD. ALL CITATIONS AVAILABLE
                                IN THE RE FORMAT
L32 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
                          2001:889341 HCAPLUS Full-text
ACCESSION NUMBER:
                          136:146764
DOCUMENT NUMBER:
                          UV Resonance Raman Study of β93-Modified
TITLE:
                          Hemoglobin A: Chemical Modifier-Specific Effects
                          and Added Influences of Attached Poly(ethylene
                          glycol) Chains
                          Juszczak, Laura J.; Manjula, Belur; Bonaventura,
AUTHOR(S):
                          Celia; Acharya, Seetharama A.; Friedman, Joel M.
                          Department of Physiology and Biophysics, Albert
CORPORATE SOURCE
                          Einstein College of Medicine, Bronx, NY, 10461,
                          Biochemistry (2002), 41(1), 376-385
 SOURCE:
                          CODEN: BICHAW; ISSN: 0006-2960
                          American Chemical Society
 PUBLISHER:
                          Journal
 DOCUMENT TYPE:
                          English
 LANGUAGE:
      The reactive sulfhydryl group on Cys \beta 93 in human adult Hb (HbA) has been the
      focus of many studies because of its importance both as a site for synthetic
      manipulation and as a possible binding site for nitric oxide (NO) in vivo.
      Despite the interest in this site and the known functional alterations associated
      with manipulation of this site, there is still considerable uncertainty as to the
      conformational basis for these effects. UV resonance Raman (UVRR) spectroscopy is
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11/091,024

used in this study to evaluate the conformational consequences of chemical modifying the Cys β93 sulfhydryl group of both the deoxy and CO-saturated derivs. of HbA using different maleimide and mixed disulfide reagents. Included among the maleimide reagents are NEM (n-ethylmaleimide) and several poly(ethylene glycol) (PEG)-linked maleimides. The PEG-based reagents include both different sizes of PEG chains (PEG2000, -5000, and -20000) and different linkers between the PEG and the maleimide. Thus, the effect on the conformation of both linker chemical and PEG size is evaluated. The spectroscopic results reveal minimal perturbation of the global structure of deoxyHbA for the mixed disulfide modification. In contrast, maleimide-based modifications of HbA perturb the deoxy T state of HbA by "loosening" the contacts associated with the switch region of the T state  $\alpha 1\beta 2$ interface but do not modify the hinge region of this interface. When the NEMmodified HbA is also subjected to enzymic treatment to remove the C-terminal Arg al41 (yielding NESdes-ArgHb), the resulting deoxy derivative exhibits the spectroscopic features associated with a deoxy R state species. All of the COsaturated derivs exhibit spectra that are characteristic of the fully liganded R structure. The deoxy and CO derivs. of HbA that have been decorated on the surface with large PEG chains linked to the maleimide-modified sulfhydryl through a short linker group all show a general intensity enhancement of the tyrosine and tryptophan bands in the UVRR spectrum. It is proposed that this effect arises from the osmotic impact of a large, close PEG mol. enveloping the surface of the protein.

RN 52-90-4 HCAPLUS

CN L-Cysteine (CA INDEX NAME)

Absolute stereochemistry.

IT 265308-62-1D, reaction products with Hb A
395676-19-4D, reaction products with Hb A
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)

(modifier-specific effects and added influences of attached poly(ethylene glycol) chains in the case of  $\beta 93$ -modified Hb A as studied by UV resonance Raman spectroscopy)

RN 265308-62-1 HCAPLUS

Poly(oxy-1,2-ethanediyl),  $\alpha-[[[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]amino]carbonyl]-<math>\omega-[[[[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]amino]carbonyl]oxy]- (9CI) (CA INDEX NAME)$ 

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RN 395676-19-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[[[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]amino]carbonyl]-<math>\omega$ -hydroxy- (CA INDEX NAME)

CC 6-3 (General Biochemistry)

IT 52-90-4, L-Cysteine, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (93; modifier-specific effects and added influences of attached poly(ethylene glycol) chains in the case of β93-modified Hb A as studied by UV resonance Raman spectroscopy)

TT 70-18-8D, Glutathione, reaction products with Hb A 128-53-0D, reaction products with Hb A 58914-60-6D, reaction products with Hb A 88504-24-9D, reaction products with Hb A 265308-62-1D, reaction products with Hb A 395676-19-4D, reaction products with Hb A

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(modifier-specific effects and added influences of attached poly(ethylene glycol) chains in the case of  $\beta 93$ -modified Hb A as studied by UV resonance Raman spectroscopy)

REFERENCE COUNT:

57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2001:256794 HCAPLUS Full-text

DOCUMENT NUMBER:

135:47625

TITLE: AUTHOR(S):

Reactive hydrogels grafted on gold surfaces Laschewsky, Andre; Ouari, Olivier; Mangeney,

Claire; Jullien, Ludovic

CORPORATE SOURCE:

Universite catholique de Louvain, Dept. of Chemistry, Louvain-la-Neuve, B-1348, Belg.

SOURCE: Macromolecular Symposia (2001),

164(Reactive Polymers), 323-340

CODEN: MSYMEC; ISSN: 1022-1360

Wiley-VCH Verlag GmbH

PUBLISHER:

DOCUMENT TYPE:

Journal

LANGUAGE:

English

Three different strategies for the fixation of stable hydrogel coatings on gold surfaces, by the grafting-to and grafting-from techniques, are described.

Monomeric or polymeric disulfide initiators are employed to start the photopolymn. of N-[tris(hydroxymethyl)methyl]acrylamide (I) via decomposition of azo compds. or via a photoredox system. Different approaches, based on the post functionalization of the poly(I) films or on copolymn. of reactive monomers with I, are employed to bind potential receptor mols. bearing amino or thiol groups as

anchor to the hydrogel. Thus, the functionalized coatings should allow the selective binding of particular analyzates. The overall goal is focused on hydrogel films for the preparation of biochips used in anal. devices such as surface plasmon resonance (SPR), though the approach seems to be generally useful for related purposes.

53918-03-9DP, reaction products with acrylamide derivative copolymers 344621-38-1DP, reaction products with 2-mercapto-5-benzimidazolesulfonate

RL: PRP (Properties); SPN (Synthetic preparation); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)

(fixation of hydrogel coatings on gold surfaces by grafting-to and grafting-from techniques)

RN 53918-03-9 HCAPLUS

CN 1H-Benzimidazole-5-sulfonic acid, 2,3-dihydro-2-thioxo-, sodium salt (1:1) (CA INDEX NAME)

Na

RN 344621-38-1 HCAPLUS

CN 2-Propenamide, N-[2-(2,5-dihydro-3,4-dimethyl-2,5-dioxo-1H-pyrrol-1-yl)ethyl]-, polymer with N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]-2-propenamide (9CI) (CA INDEX NAME)

CM 1

CRN 249621-29-2 CMF C11 H14 N2 O3

$$CH_2-CH_2-NH-C-CH=CH_2$$

$$O$$

$$Me$$

$$Me$$

CM 2

CRN 13880-05-2 CMF C7 H13 N O4

IT 344621-38-1P

RL: PRP (Properties); SPN (Synthetic preparation); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)

(preparation of macroinitiator for fixation of hydrogel coatings on gold surfaces by grafting-to and grafting-from techniques)

RN 344621-38-1 HCAPLUS

CN 2-Propenamide, N-[2-(2,5-dihydro-3,4-dimethyl-2,5-dioxo-1H-pyrrol-1-yl)ethyl]-, polymer with N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]-2-propenamide (9CI) (CA INDEX NAME)

CM 1

CRN 249621-29-2 CMF C11 H14 N2 O3

CM 2

CRN 13880-05-2 CMF C7 H13 N O4

CC 42-2 (Coatings, Inks, and Related Products)

IT 53918-03-9DP, reaction products with acrylamide derivative copolymers 344621-38-1DP, reaction products with

2-mercapto-5-benzimidazolesulfonate

33

RL: PRP (Properties); SPN (Synthetic preparation); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)

(fixation of hydrogel coatings on gold surfaces by grafting-to and grafting-from techniques)

IT 344621-38-1P

RL: PRP (Properties); SPN (Synthetic preparation); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)

(preparation of macroinitiator for fixation of hydrogel coatings on gold surfaces by grafting-to and grafting-from techniques)

REFERENCE COUNT:

THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

11/091.024

80

L32 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:95555 HCAPLUS Full-text

DOCUMENT NUMBER: 135:13817

TITLE: Enhancement of gene delivery by an analogue of

α-MSH in a receptor-independent fashion

AUTHOR(S): Chluba, J.; Lima de Souza, D.; Frisch, B.;

Schuber, F.

CORPORATE SOURCE: Laboratoire de Chimie Bioorganique, UMR 7514

CNRS-ULP, Faculte de Pharmacie, Illkirch, 67400,

Fr.

SOURCE: Biochimica et Biophysica Acta, Biomembranes (

2001), 1510(1-2), 198-208

CODEN: BBBMBS; ISSN: 0005-2736

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

In order to transfect melanoma specifically by receptor-mediated endocytosis we AB prepared dioctadecyl aminoglycylspermine (lipospermine)-DNA complexes with [Nle4,D-Phe7]- $\alpha$ -MSH(4-10), a pseudo-peptide analog of  $\alpha$ -MSH ( $\alpha$ -MSH) linked to a thiol-reactive phospholipid. With these complexes we obtained an up to 70-fold increase of transfection with B16-F1 melanoma cells. However when B16-G4F, an  $\alpha$ -MSH receptor neg. melanoma cell line was transfected, an up to 700-fold increased transfection efficiency was observed The peptide hormone analog was equally efficient when it was only mixed with lipospermine-DNA complexes without covalent In addition to melanoma cells we also obtained up to 30-fold increased transfection with BN cells (embryonic liver cells). Our data show that an  $\alpha\textsc{-MSH}$ analog increased transfection independently of the MSH receptor expression but reaches efficiencies approaching those obtained with peptides derived from viral fusion proteins. The absence of targeting of constructs containing [Nle4,D-Phe7]- $\alpha$ -MSH(4-10) can probably be attributed due to the relatively modest number of MSH receptors at the surface of melanoma. We suggest, however, that the peptide hormone analog used in this study has membrane-active properties and could be of interest as helper agent to enhance non-viral gene delivery presumably by endosomal-destabilizing properties.

IT 342643-63-4 342643-64-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(enhancement of gene delivery by analog of α-MSH in

receptor-independent fashion)

RN 342643-63-4 HCAPLUS

CN Glycinamide, N=(3-mercapto-1-oxopropyl)glycyl-L-norleucyl-L-\alpha = d d glutamyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

RN 342643-64-5 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]-ω-[[7-hydroxy-7-oxido-2,13-dioxo-10-[(1-oxohexadecyl)oxy]-6,8,12-trioxa-3-aza-7-phosphaoctacos-1-yl]oxy]-(9CI) (CA INDEX NAME)

PAGE 1-A

$$\begin{array}{c|c} CH_2-CH_2 & \hline \\ O-,CH_2-CH_2 & \hline \\ O & O \end{array}$$

PAGE 1-B

IT 342643-65-6DP, lipospermine-DNA complex

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(enhancement of gene delivery by analog of  $\alpha\textsc{-MSH}$  in receptor-independent fashion)

RN 342643-65-6 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[7-hydroxy-7-oxido-2,13-dioxo-10-[(1-oxohexadecyl)oxy]-6,8,12-trioxa-3-aza-7-phosphaoctacos-1-yl]-ω-hydroxy-, ether with N-[3-[[1-(2-hydroxyethyl)-2,5-dioxo-3-pyrrolidinyl]thio]-1-oxopropyl]glycyl-L-norleucyl-L-α-glutamyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophylglycinamide (9CI) (CA INDEX, NAME)

## PAGE 2-B

$$CH_2-CH_2-O$$
 $CH_2-CH_2-O$ 
 $CH_2-CH_2-O$ 
 $CH_2-CH_2-O$ 
 $CH_2-CH_2-O$ 
 $CH_2-CH_2-O$ 
 $CH_2-CH_2-O$ 

- CC 1-2 (Pharmacology)
  - Section cross-reference(s): 63
- IT 342643-63-4 342643-64-5
  - RL: RCT (Reactant); RACT (Reactant or reagent)

(enhancement of gene delivery by analog of  $\alpha\textsc{-MSH}$  in receptor-independent fashion)

- IT 342643-65-6DP, lipospermine-DNA complex
  - RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)

(enhancement of gene delivery by analog of  $\alpha\textsc{-MSH}$  in

## receptor-independent fashion)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2001:78501 HCAPLUS Full-text

DOCUMENT NUMBER: 134:14387.6

Protease conjugates having sterically protected epitope regions and their uses in cleaning and

personal care compositions

/ENTOR(S): INVENTOR(S):

Rubingh, Donn Nelton; Weisgerber, David John;

Correa, Paul Elliott

PATENT ASSIGNEE(S): The Procter & Gamble Company, USA SOURCE: PCT Int. Appl., 40 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007577	A2	20010201	WO 2000-US18854	200007
CN, CR, CU, GM, HR, HU, LR, LS, LT, PL, PT, RO, UA, UG, UZ, RW: GH, GM, KE, CY, DE, DK,	AM, AT CZ, DE ID, IL LU, LV RU, SD VN, YU LS, MW ES, FI CG, CI	, AU, AZ, , DK, DM, , IN, IS, , MA, MD, , SE, SG, , ZA, ZW , MZ, SD, , FR, GB, , CM, GA,	BA, BB, BG, BR, BY, DZ, EE, ES, FI, GB, JP, KE, KG, KP, KR, MG, MK, MN, MW, MX, SI, SK, SL, TJ, TM, SL, SZ, TZ, UG, ZW, GR, IE, IT, LU, MC, GN, GW, ML, MR, NE,	GD, GE, GH, KZ, LC, LK, MZ, NO, NZ, TR, TT, TZ, AT, BE, CH, NL, PT, SE,
				11
BR 2000012692	A	20020409	BR 2000-12692	200007 11
EP 1196547	A2	200204,17	EP 2000-945317	200007b
R: AT, BE, CH,			GB, GR, IT, LI, LU,	NL, SE, MC,

PT, IE, SI, LT, LV, FI, RO JP 2003505069 T 20030212 JP 2001-512848

200007

20041021

200007 , 11

US 6946128

B1 20050920

US 2000-618235

200007

PRIORITY APPLN. INFO.

US 1999-144979P

199907

22

WO 2000-US18854

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200007

11

The present disclosure relates to subtilisin protease conjugate comprising a protease moiety and one or more addition moieties. Each addition moiety is covalently attached to an epitope protection position of the protease moiety. The protease conjugates have decreased immunogenicity relative to a parent protease. The present disclosure further relates to cleaning and personal care compns. comprising the protease conjugates.

IT 244287-84-1-322725-90-6

Barrell !

RL: RCT (Reactant); RACT (Reactant or reagent)
(protease conjugates having sterically protected epitope regions and their uses in cleaning and personal care compns.)

RN 244287-84-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[2-[[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]amino]-2-oxoethyl]- $\omega$ -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH2-NH-C-CH2 & O-CH2-CH2 \\ \hline \\ O-CH2-CH2 & n \end{array}$$

RN 322725-90-6, HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α,α'-[[(1S)-1-[[[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethyl]amino]carb onyl]-1,5-pentanediyl]bis(iminocarbonyl)]bis[ω-methoxy- (CA INDEX NAME)

PAGE 1-B

$$-CH_2 - OMe$$

$$-O-CH_2 - CH_2 - OMe$$

TT 52-90-4, Cysteine, biological studies
RL: BOC (Biological occurrence); BSU (Biological study,
unclassified); RCT (Reactant); BIOL (Biological study); OCCU
(Occurrence); RACT (Reactant or reagent)
(substituting amino acid; protease conjugates having sterically
protected epitope regions and their uses in cleaning and personal
care compns.)

RN 52-90-4 HCAPLUS

CN L-Cysteine (CA INDEX NAME)

Absolute stereochemistry.

ICM C12N009-00 IC CC 7-8 (Enzymes) Section cross-reference(s): 46, 62 IT Polyoxyalkylenes, biological studies RL: BUU (Biological use, unclassified); NUU (Other use, and the state of the state unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses) (conjugates with proteinases; protease conjugates having sterically protected epitope regions and their uses in cleaning and personal care compns.) IT Polymers, biological studies RL: BUU (Biological use, unclassified); NUU (Other use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses) (conjugates, with proteases; protease conjugates having sterically protected epitope regions and their uses in cleaning and personal care compns.) 541-59-3D, Maleimide, alkyl derivs. 244287-84-1 IT 322725-9046 RL: RCT (Reactant); RACT (Reactant or reagent) (protease conjugates having sterically protected epitope regions and their uses in cleaning and personal care compns.) IT 52-90-4, Cysteine, biological studies RL: BOC (Biological occurrence); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); OCCU (Occurrence); RACT (Reactant or reagent)

(substituting amino acid; protease conjugates having sterically decided by

protected epitope regions and their uses in cleaning and personal

L32 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2001:78425 HCAPLUS Full-text

care compns.)

```
DOCUMENT NUMBER:
                          134:143874
TITLE:
                          Protease conjugates having sterically protected
                          clip sites and reduced immunogenicity and their
                          use in cleaning and personal care compositions
                          Weisgerber, David John; Rubingh, Donn Nelton;
INVENTOR(S):
                          Correa, Paul Elliott
PATENT ASSIGNEE(S):
                          The Procter & Gamble Company, USA
SOURCE:
                          PCT Int. Appl., 38 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:
                          Patent
LANGUAGE:
                          English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
   الأربع المعور والأشاء وسعة إلما لما يما
     PATENT NO.
                          KIND
                                              APPLICATION NO.
     WO 2001007484
                                                                。 使用人的人 医皮脂醇 医环
                           A2
                                  20010201
                                              WO 2000-US18855
                                                                      200007
         O01007484 A3 20010607
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES,
     WO 2001007484
             FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
             KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,
             MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
        BE, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                 20010201
                                             CA 2000-2379729
   CA 2379729
                           Α1
                                                                       200007
     BR 2000012694
                                  20020409
                                              BR 2000-12694
                                                                      200007
    EP 1196548
                                 20020417
                                              EP 2000-945318
                           A2 .
                                                                      200007
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
            PT, IE, SI, LT, LV, FI, RO
     JP 2003516116
                                 20030513
                                              JP 2001-512566
                                                                      200007
                                                                     US 6566115 B1
                                  20030520
                                              US 2000-618740
                                                                     200.007
PRIORITY APPLN. INFO.:
                                              US 1999-144981P
                                                                     199907
                                                                       22
                                                    <--
                                              WO 2000-US18855
```

The present disclosure relates to subtilisin protease conjugate comprising a protease moiety and one or more addition moieties. Each addition moiety is covalently attached to a clip site protection position of the protease moiety, wherein the clip site protection positions are selected from 13, 14, 15, 16, 18, 19, 20, 21, 84, 85, 88, 158, 159, 160, 161, 162, 163, 164, 165, 170, 186, 191, 192, 193; 194, 196, 259, 260, 261, 262, and 274 corresponding to subtilisin BPN. The protease conjugates have decreased immunogenicity relative to a parent protease. The present disclosure further relates to cleaning and personal care compns. comprising the protease conjugates.

IT 244287-84-1 322725-90-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(protease conjugates having sterically protected clip sites and
reduced immunogenicity and their use in cleaning and personal
care compns.)

RN 244287-84-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[2-[[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]amino]-2-oxoethyl]-<math>\omega$ -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH2-NH-C-CH2 & \boxed{ } O-CH2-CH2 & \boxed{ } n \end{array}$$
 OMe

RN 322725-90-6 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α,α'-[[(1S)-1-[[[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethyl]amino]carb onyl]-1,5-pentanediyl]bis(iminocarbonyl)]bis[ω-methoxy- (CA INDEX NAME)

PAGE 1-B

$$-CH_2 - OMe$$

$$O-CH_2 - CH_2 - OMe$$

52-90-4, Cysteine, biological studies RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent) (substituting amino acid; protease conjugates having sterically protected clip sites and reduced immunogenicity and their use in cleaning and personal care compns.) RN 52-90-4 HCAPLUS CN L-Cysteine (CA INDEX NAME) Absolute stereochemistry. NH2' IC ICM C07K017-00 CC 7-8 (Enzymes) Section cross-reference(s): 46, 62, 63 Polyoxyalkylenes, biological studies RL: BUU (Biological use, unclassified); NUU (Other use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses) (conjugates with protease; protease conjugates having sterically) protected clip sites and reduced immunogenicity and their use in cleaning and personal care compns.) IT Polymers, biological studies RL: BUU (Biological use, unclassified); NUU (Other use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses) (conjugates, with protease; protease conjugates having sterically protected clip sites and reduced immunogenicity and their use single of cleaning and personal care compns.) IT 541-59-3D, Maleimide, alkyl derivs. 244287-84-1 322725-90-6 RL: RCT (Reactant); RACT (Reactant or reagent) (protease conjugates having sterically protected clip sites and and the reduced immunogenicity and their use in cleaning and personal care compns.) 52-90-4, Cysteine, biological studies IT RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent) (substituting amino acid; protease conjugates having sterically protected clip sites and reduced immunogenicity and their use in cleaning and personal care compns.) L32 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN 2000:314735 HCAPLUS Full-text ACCESSION NUMBER: DOCUMENT NUMBER: Modification of anti-integrin antibodies and TITLE: antibody fragments for improved pharmacokinetics Heavner, George A.; Weber, Robert W. INVENTOR(S): PATENT ASSIGNEE(S): Centocor, Inc., USA SOURCE: PCT Int. Appl., 83 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent

English

LANGUAĜE:

FAMILY ACC. NUM. COUNT:

## PATENT INFORMATION:

PAT	ENT NO.	KIND	DATE	APPLICATION NO.	DATE
	10 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1				
. WO	2000026256	A2	20000511	WO 1999-US25790	
					199911 02
				,	02
WO	2000026256	A3	20011108	<b>&lt;</b>	· 中国的自己的特殊的。
	2000026256		20011108		
				BB, BG, BR, BY, CA,	CH. CN. CR.
	CU, CZ, DE,	DK, DM	, EE, ES,	FI, GB, GD, GE, GH,	GM, HR, HU,
	ID, IL, IN,	IS, JP	, KE, KG,	KP, KR, KZ, LC, LK,	LR, LS, LT,
				MW, MX, NO, NZ, PL,	
			, SL, TJ,	TM, TR, TT, TZ, UA,	UG, US, UZ,
	VN, YU, ZA,		SD SI	SZ, TZ, UG, ZW, AT,	BF CH CV
				IE, IT, LU, MC, NL,	
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EP .	1144452	A3	20020313		
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11/091.024

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The authors disclose the modification of antibodies for improved pharmacokinetics. The antibodies bind to one or more human integrin receptors selected from the group consisting of GPIIb/IIIa,  $\alpha\nu\beta3$  and Mac-1. The modifications comprise organic moieties which are covalently bonded to specific sites on the antibodies. The organic moieties can be hydrophilic polymers, fatty acid groups, fatty acid ester groups, lipids or phospholipids. Also disclosed is treatment of diseases or disorders in which cells expressing GPIIb/IIIa,  $\alpha\nu\beta3$  and/or Mac-1 play a pathophysiol. role.

IT 267431-72-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(conjugation with antibody)

RN 267431-72-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[2-[[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)acetyl]amino]ethyl]- $\omega$ -[2-[(1-oxohexadecyl)amino]ethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A  $CH_2 - C - NH - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - NH - CH_2 - CH_2 - CH_2 - NH - CH_2 - CH_2$ 

PAGE 1-B

- (CH2)14-Me

IT 52-90-4, L-Cysteine, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified);
BIOL (Biological study); PROC (Process)

(for modification within anti-integrin antibodies and antibody fragments for improved pharmacokinetics)

RN 52-90-4 HCAPLUS

CN L-Cysteine (CA INDEX NAME)

Absolute stereochemistry.

IC ICM C07K016-00

CC 15-3 (Immunochemistry)

Section cross-reference(s): 1, 14

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Polymers, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified);

PRP (Properties); THU (Therapeutic use); BIOL (Biological study);

PROC (Process); USES (Uses)

(conjugates, with anti-integrin antibodies; improved

pharmacokinetics of)

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IT Fatty acids, biological studies
     Lipids, biological studies
     Phospholipids, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified);
     PRP (Properties); THU (Therapeutic use); BIOL (Biological study);
     PROC (Process); USES (Uses)
       (conjugates, with polyethylene glycol; for modification of
        anti-integrin antibodies and antibody fragments for improved
        pharmacokinetics)
   Fatty acids, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified);
     PRP (Properties); THU (Therapeutic use); BIOL (Biological study);
     PROC (Process); USES (Uses)
        (esters, conjugates, with polyethylene glycol; for modification
        of anti-integrin antibodies and antibody fragments for improved
        pharmacokinetics)
IT
     Oligosaccharides, biological studies
     Polyoxyalkylenes, biological studies
    Polysaccharides, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified);
     BIOL (Biological study); PROC (Process)
        (for modification of anti-integrin antibodies and antibody
       fragments for improved pharmacokinetics)
IT
     Polyamides, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified);
     BIOL (Biological study); PROC (Process)
        (poly(amino acids); for modification of anti-integrin antibodies
        and antibody fragments for improved pharmacokinetics)
   267431-72-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
     RACT (Reactant or reagent)
        (conjugation with antibody)
IT
     52-90-4, L-Cysteine, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified);;
     BIOL (Biological study); PROC (Process)
        (for modification within anti-integrin antibodies and antibody
        fragments for improved pharmacokinetics)
L32 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                         2000:156739 HCAPLUS Full-text
DOCUMENT NUMBER:
                         132:304797
                         Cys-93-\beta\beta-succinimidophenyl
                         polyethylene glycol 2000 hemoglobin A.
                         Intramolecular cross-bridging of hemoglobin
                         outside the central cavity
                         Manjula, Belur N.; Malavalli, Ashok; Smith, Paul
AUTHOR(S):
                         K.; Chan, Nei-Li; Arnone, Arthur; Friedman, Joel
                         M.; Acharya, A. Seetharama
                         Departments of Physiology and Biophysics, Albert
CORPORATE SOURCE:
                         Einstein College of Medicine, Bronx, NY, 10461,
                         Journal of Biological Chemistry (2000)
                         1), 275(8), 5527-5534
                         CODEN: JBCHA3; ISSN: 0021-9258
                         American Society for Biochemistry and Molecular
PUBLISHER:
                         Biology
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
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11/091,024

Bis(maleidophenyl)-PEG2000 (Bis-Mal-PEG2000), a new bifunctional protein cross-AB linker targeted to sulfhydryl groups, introduces intra-tetrameric cross-links into oxy-HbA in nearly quant. yields. Structural as well as crystallog analyses of the cross-linked species, Bis-Mal-PEG2000 HbA, identified Cys-93(\$) as the site of intramol. crosslinking. The cross-bridging had only a limited influence on the O2 affinity and cooperativity of HbA in 50 mM BisTris acetate, pH 7.4. However, the Bohr effect was reduced by .apprx.60%. Bis-Mal-PEG2000 HbA retained sensitivity to the presence of allosteric effectors 2,3-diphosphoglycerate, IHP, and chloride, albeit to a lesser degree compared with HbA. Crystallog, anal. revealed the overall structure of deoxy-Bis-Mal-PEG2000 HbA to be similar to deoxy-HbA but for the loss of the salt bridge between Asp-94( $\beta$ ) and His-146( $\beta$ ). The large influence of the cross-bridging on the alkaline Bohr effect of HbA is consistent with the loss of this salt bridge. Unlike the "central cavity cross-bridges" described previously, the cross-link introduced by Bis-Mal-PEG2000 into HbA is an "outside the central cavity cross-bridge.". In view of its oxy-conformational specificity and limited influence on O2 affinity, this new crosslinking strategy holds promise for the stabilization of new designer low O2 affinity Hbs generated by recombinant DNA technol. for applications as Hb based therapeutics.

IT 52-90-4, L-Cysteine, reactions

RN 52-90-4 HCAPLUS

CN L-Cysteine (CA INDEX NAME)

超级绝数 副进门

Absolute stereochemistry.

IT 265308-62-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intramol. cross-bridging of Hb outside the central cavity results from reaction of bis(maleidophenyl)-PEG2000 with Cys93( $\beta$ ) residues of Hb A)

RN 265308-62-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha-[[[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]amino]carbonyl]-<math>\omega-[[[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]amino]carbonyl]oxy]- (9CI) (CA INDE) NAME)$ 

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CC 6-3 (General Biochemistry)

Section cross-reference(s): 75

IT 56-84-8, L-Aspartic acid, biological studies 71-00-1,

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L-Histidine, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified)
     BIOL (Biological study); PROC (Process)
        (cross-bridging reaction of bis(maleidophenyl)-PEG2000 with
        Cys93(\beta) residues of Hb A causes disruption of salt bridge.
        between Asp94(\beta) and His146(\beta))
     52-90-4, L-Cysteine, reactions
                                      9034-51-9, Hemoglobin A
     25322-68-3 123457-83-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (intramol. cross-bridging of Hb outside the central cavity)
        results from reaction of bis(maleidophenyl)-PEG2000 with
        Cys93(B) residues of Hb A)
IT
     265308-62-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
     RACT (Reactant or reagent)
        (intramol. cross-bridging of Hb outside the central cavity
        results from reaction of bis(maleidophenyl)-PEG2000 with
        Cys93(\beta) residues of Hb A)
REFERENCE COUNT:
                               THERE ARE 30 CITED REFERENCES AVAILABLE
                               FOR THIS RECORD. ALL CITATIONS AVAILABLE
                               IN THE RE FORMAT
L32 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                         1998:678095 HCAPLUS Full-text
DOCUMENT NUMBER:
                         130:38746
TITLE:
                         Synthesis of water-soluble, nonimmunogenic
                         polyamide crosslinking agents
                         Hai, Ton That; Pereira, David E.; Nelson, Deanna
AUTHOR (S):
CORPORATE SOURCE: ,
                         Hemoglobin Therapeutics Division, Baxter
                         Healthcare Corp., Round Lake, IL, 60073, USA
SOURCE:
                         Bioconjugate Chemistry (1998), 9(6),
                         645-654
                         CODEN: BCCHES; ISSN: 1043-1802
                         American Chemical Society
PUBLISHER:
DOCUMENT : TYPE:
                         Journal
LANGUAGE:
                         English
AB
     Novel polyamides were developed that can be used as crosslinking agents for
     proteins such as Hb.
                           Water-soluble, nonimmunogenic polyamides containing oxygen
     and sulfur atoms in the backbone were prepared by the polycondensation of the
     diacids bis(carboxymethyloxyacetyl)-1,4-diaminobutane or 3,3'-thiodipropionic acid
     (1b) with diethylene glycol bis(3-aminopropyl) ether. The resulting \alpha, \omega-diacids
     were converted to the corresponding activated esters using any of a variety of
     carboxylic acid activating reagents including the novel reagent diphenyl(1-
     methylimidazol-2-thiyl)phosphonate. The resulting polyamides could be activated
     with a broad spectrum of groups that allow for the crosslinking and surface
     modification of proteins.
     60-56-0, 2-Mercapto-1-methylimidazole
IT
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (diacid activating reagent synthesis; preparation of water-soluble,
        nonimmunogenic polyamide crosslinking agents)
RN
     60-56-0 HCAPLUS
     2H-Imidazole-2-thione, 1,3-dihydro-1-methyl- (CA INDEX NAME)
CN
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IT 216884-38-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of water-soluble, nonimmunogenic polyamide crosslinking, agents)

RN 216884-38-7 HCAPLUS

CN Poly[oxy-1,2-ethanediyloxy-1,2-ethanediyloxy-1,3-propanediylimino(1oxo-1,2-ethanediyl)oxy(2-oxo-1,2-ethanediyl)imino-1,4butanediylimino(1-oxo-1,2-ethanediyl)oxy(2-oxo-1,2-ethanediyl)imino-1
1,3-propanediyl], α-[3-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1yl)-1-oxopropyl]amino]propyl]-ω-[2-[2-[3-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]propoxy]ethoxy](9CI) (CA INDEX NAME)

PAGE 1-C

O

NH-(CH2)3-NH-C-CH2-CH2-O-(CH2)3-NH-C-CH2-

PAGE 1-D

35-5 (Chemistry of Synthetic High Polymers)

7.排尿病, ser 注 图 2 字

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Section cross-reference(s): 33, 63
IT 60-56-0, 2-Mercapto-1-methylimidazole
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (diacid activating reagent synthesis; preparation of water-soluble,
       nonimmunogenic polyamide crosslinking agents)
     108-30-5DP, Succinic anhydride, reaction products with polyamides
IT
     6066-82-6DP, N-Hydroxysuccinimide, reaction products with polyamides
     55750-62-4DP, N-Succinimidyl 3-maleimidopropionate, reaction
    products with polyamides
                              74124-79-1DP, N,N'-Disuccinimidyl
    carbonate, reaction products with polyamides
                                                157069-29-9DP,
   reaction products with activation agents: 216884-32-1P
                                 216884-36-5DP, reaction products with
    216884-33-2P 216884-35-4P
    activation agents 216884-38-7P
                                    216884-39-8P
    216884-40-1P 216884-41-2P
                                 216884-42-3DP, reaction products with
    activation agents 216884-43-4DP, reaction products with
    succinimide derivs. 216884-44-5P 216884-45-6P
    RL: SPN (Synthetic preparation); PREP (Preparation)
       (preparation of water-soluble, nonimmunogenic polyamide crosslinking
                             THERE ARE 17 CITED REFERENCES AVAILABLE
REFERENCE COUNT:
                        17
                             FOR THIS RECORD. ALL CITATIONS AVAILABLE
                             IN THE RE FORMAT
L32 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                       1998:300866 HCAPLUS Full-text
DOCUMENT NUMBER:
                        129:4872
TITLE:
                        Preparation of targetable diagnostic and
                        therapeutic gas-containing or gas-generating
                        ultrasound contrast agents
INVENTOR(S):
                        Klaveness, Jo; Rongved, Pal; Hogset, Anders;
                        Tolleshaug, Helge; Naevestad, Anne; et al.
PATENT ASSIGNEE(S):
                        Marsden, John Christopher, UK; Nycomed Imaging
                        AS
                        PCT Int. Appl., 205 pp.
                       CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
    PATENT NO.
                        KIND
                              DATE
                                          APPLICATION NO.
    WO 9818501 A2
                              19980507
                                          WO 1997-GB2954
                                                                199710
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    WO 9818501 A3
                              19980730
     W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP,
            KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO,
            NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
            UA, UG, US, UZ, VN, YU, ZW, BA, MK, SZ, BE, FR, GR, IE, IT,
            MC, NL, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD,
            TG ...
        RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
            FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
           CM, GA, GN, ML, MR, NE, SN, TD, TG
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EP 1998-917461
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US 2001-925715
                       # 200108
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Targetable diagnostic and/or therapeutically active agents, e.g. ultrasound contrast agents, comprising a suspension in an aqueous carrier liquid of a reporter comprising gas-containing or gas-generated material, in which the reporter is coupled or linked to one or more non-bloactive vectors. Thus, a mixture of phosphatidylserine, phosphatidylcholine, and biotinamidocaproate-PEG3400-I-Ala- cholesterol (preparation given) was dispersed in 5% propylene glycol-water, flushed with perfluorobutane, and sonicated to give gas-filled encapsulated microbubbles.

IT 207403-10-9P

207403-10-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of targetable diagnostic and therapeutic gas-containing or gas-generating ultrasound contrast agents linked to non-bioactive vectors)

RN 207403-10-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[6-hydroxy-6-oxido-1,12-dioxo-9-['(1-oxooctadecyl')oxy]-5,7,11-trioxa-2-aza-6-phosphanonacos-1-yl]-  $\omega$ -[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
CH_2 - CH_2 - C - NH - CH_2 - CH_2 - O - CH_2 - CH_2 - O - NH - CH_2 - O - CH_2$$

PAGE 1-E

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IT 207302-63-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of targetable diagnostic and therapeutic gas-containing or gas-generating ultrasound contrast agents linked to non-bioactive vectors)

RN 207302-63-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[6-hydroxy-6-oxido-1,12-dioxo-9[(1-oxooctadecyl)oxy]-5,7,11-trioxa-2-aza-6-phosphanonacos-1-yl]ω-hydroxy-, ether with L-arginylglycyl-L-α-aspartyl-S-[1[3-[(2-hydroxyethyl)amino]-1-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]-Lcysteine (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

$$-CH_{2} - CH_{2} -$$

PAGE 1-C

2008年,在1986年度2008年

IT 62571-86-2, Captopril

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of targetable diagnostic and therapeutic gas-containing or gas-generating ultrasound contrast agents linked to non-bloactive vectors)

RN 62571-86-2 HCAPLUS

CN L-Proline; (1-[)(2S)-3-mercapto-2-methyl-1-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IC A61K051-08; A61K051-10; A61K049-00; A61K047-48

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 9, 63

IT Phosphatidylcholines, biological studies

Phosphatidylserines

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of targetable diagnostic and therapeutic gas-containing or gas-generating ultrasound contrast agents linked to non-bioactive vectors)

IT 207403-10-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of targetable diagnostic and therapeutic gas-containing or gas-generating ultrasound contrast agents linked to non-bioactive vectors)

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        gas-generating ultrasound contrast agents linked to non-bloactive
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     59-05-2, Methotrexate 59-30-3, Folic acid, biological
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     3',5'-Di-O-palmitoyl-5-fluoro-2'-deoxyuridine
                                                     9002-07-7D, Trypsin,
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                                      9013-20-1, Streptavidin.
     25104-18-1, L-Lysine homopolymer
                                        38000-06-5, Poly-L-lysine, SRU
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     62571-86-2, Captopril
     RL: BAC (Biological activity or effector, except adverse); BSU
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     (Biological study); USES (Uses)
        (preparation of targetable diagnostic and therapeutic gas-containing or
        gas-generating ultrasound contrast agents linked to non-bioactive
L32 ANSWER 22: OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                        1998:300865 HCAPLUS Full-text
DOCUMENT NUMBER:
                         129:4871
TITLE:
                         Preparation of targetable diagnostic and
                         therapeutic gas-containing or gas-generating
                         ultrasound contrast agents
                         Klaveness, Jo; Rongved, Pal; Hogset, Anders;
INVENTOR ('S'):
                         Tolleshaug, Helge; Cuthbertson, Alan; et al.; et
                         al.
PATENT ASSIGNEE(S):
                         Marsden, John Christopher, UK; Nycomed Imaging
SOURCE:
                         PCT Int. Appl., 150 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
                         10.
PATENT INFORMATION:
     PATENT NO.
                                            APPLICATION NO.
     WO 9818500
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                                19980507
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         W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
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             NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
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             NL, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
       RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
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Targetable diagnostic and/or therapeutically active agents, e.g. ultrasound contrast agents, comprising a suspension in an aqueous carrier liquid of a reporter comprising gas-containing or gas-generated material, in which the reporter is coupled or linked to one or more non-bioactive vectors. Thus, lipopeptide R-Lys(R)-Lys-Arg-Lys-Arg- Trp-Glu-Pro-Pro-Arg-Ala-Arg-Ile-OH (I; R = hexadecanoyl) (preparation given) containing a heparin binding site and a fibronectin binding site, was prepared by standard solid-phase methods. Microbubbles containing lipopeptide I were tested in vitro for binding to endothelial cells under flow conditions.

IT 207302-63-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of targetable diagnostic and therapeutic gas-containing or gas-generating ultrasound contrast agents linked to non-bloactive vectors)

RN 207302-63-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[6-hydroxy-6-oxido-1,12-dioxo-9[(1-oxooctadecyl)oxy]-5,7,11-trioxa-2-aza-6-phosphanonacos-1-yl]ω-hydroxy-, ether with L-arginylglycyl-L-α-aspartyl-S-[1[3-[(2-hydroxyethyl)amino]-1-oxopropyl]-2,5-dioxo-3-pyrrolidinyl]-Lcysteine (9CI) (CA INDEX NAME)

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PAGE 1-B

PAGE 1-C

IT 62571-86-2, Captopril

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of targetable diagnostic and therapeutic gas-containing or gas-generating ultrasound contrast agents linked to non-broactive vectors)

RN 62571-86-2 HCAPLUS

CN L-Proline, 1-[(2S)-3-mercapto-2-methyl-1-oxopropyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 207403-10-9P

· (1) 建筑 医二种原理的

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of targetable diagnostic and therapeutic gas-containing or gas-generating ultrasound contrast agents linked to non-bioactive vectors)

RN 207403-10-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl),  $\alpha$ -[6-hydroxy-6-oxido-1,12-dioxo-9-[-(1-oxooctadecyl)oxy]-5,7,11-trioxa-2-aza-6-phosphanonacos-1-yl]- $\omega$ -[2-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

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IC
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     ICS A61K051-10; A61K049-00; A61K047-48
CC
    34-3 (Amino Acids, Peptides, and Proteins)
IT
     Phosphatidylcholines, biological studies
     Phosphatidylserines
     RL: BAC (Biological activity or effector, except adverse); BSU
     (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (preparation of targetable diagnostic and therapeutic gas-containing or
        gas-generating ultrasound contrast agents linked to non-bioactive
        vectors)
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    RL: BAC (Biological activity or effector, except adverse); BSU
     (Biological study, unclassified); SPN (Synthetic preparation); THU
    (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES,
     (Uses)
       (preparation of targetable diagnostic and therapeutic gas-containing or
        gas-generating ultrasound contrast agents linked to non-bioactive
        vectors)
IT
     1405-20-5, Polymixin B sulfate
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    38000-06-5, Poly-L-lysine, SRU 62571-86-2, Captopril
     RL: BAC (Biological activity or effector, except adverse); BSU
     (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (preparation of targetable diagnostic and therapeutic gas-containing or
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    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
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    ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
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DOCUMENT NUMBER:

127:322794

Property-affecting and/or property-exhibiting compositions for therapeutic and diagnostic uses Rabbani, Elazar; Stavrianopoulos, Jannis G.; Donegan, James J.; Liu, Dakai; Kelker, Norman

ACCESSION NUMBER:

1997:667263 HCAPLUS Full-text

Barrell St.

E.; Engelhardt, Dean L.
PATENT ASSIGNEE(S): Enzo Therapeutics, Inc., USA SOURCE: Can. Pat. Appl., 275 pp.

CODEN: CPXXEB Patent

DOCUMENT TYPE:

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
CA 2190304	<b>A1</b>	19970616	CA 1996-2190304		199611
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CA 2279669	<b>A1</b>	19970616	CA 1996-2279669		199611
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Compns. useful for effecting and/or exhibiting changes in biol. functioning and AΒ processing in cells and biol . systems are provided which combine chemical modifications and/or ligand addns. with biol. functions in such a way as not to interfere substantially with the biol. functions. Such addnl. characteristics include nuclease resistance, targeting specific cells or cell receptors, and augmenting or decreasing interactions between the compns. and target cells. A title composition may constitute a nucleotide, nucleotide analog, nucleic acid, natural or synthetic polymer, ligand, or conjugate of a ligand with any of the preceding. For example, single-stranded DNA from a plasmid containing a gene of interest is complexed with an allylamine phosphoramidite-containing oligonucleotide primer (complementary to a region of the DNA distant from the gene of interest) which as been modified with trilactosyllysyllysine (preparation given), and the primer is extended with Klenow enzyme to form completely doublestranded DNA. On exposure of target cells to this DNA, the galactose moieties on the DNA bind to receptors on the cells, resulting in transport of the DNA into the cell's. Invanother embodiment, DNA for antisense RNA sequences to regions of the HIV genome were inserted into the Ul small nuclear RNA coding region and the DNA was used to transform U937 cells. The transformed cells were resistant to HIV infection, as shown by inhibition of virus replication and p24 antigen production

RL: RCT (Reactant); RACT (Reactant or reagent)

(property-affecting and/or property-exhibiting compns. for

therapeutic and diagnostic uses)

1 1 m

RN 197431-06-4 HCAPLUS

197431-06-4

TΨ

CN 2,3-Butanediol, 1-[(4,5-diamino-2-hydroxycyclohexyl)thio]-4-mercapto-(9CI) (CA INDEX NAME)

海中海 电电影

IT 197526-75-3P 197526-77-5P

医乳质 海洲地區科

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

· (property-affecting and/or property-exhibiting compns. for

therapeutic and diagnostic uses)

RN 197526-75-3 HCAPLUS

CN 5'-Adenylic acid, 2'-deoxy-, homopolymer, 5'→3'-ester with
5'-[[3-[3-[4-[[4,5-bis[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1oxopropyl]amino]-2-hydroxycyclohexyl]thio]-2,3-dihydroxybutyl]thio]2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]-2',5'-dideoxyadenosine
(9CI) (CA INDEX NAME)

, CM = 1

CRN 197431-08-6

CMF C41 H51 N11 014 S2

4. "高级原则"

Absolute stereochemistry.

CM 2

CRN 25191-20-2

CMF (C10, H14 N5 06 P)x

CCI PMS

CM 3

CRN 653-63-4

CMF C10 H14 N5 O6 P

Absolute stereochemistry. Rotation (+).

PAGE 1-R

RN 197526-77-5 HCAPLUS

CN 5:-Thymidylic acid, homopolymer, 5:→3'-ester with 5:-[[3-[3+[4-[4,5-bis[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-y1)-1-oxopropyl]amino]-2-hydroxycyclohexyl]thio]-2,3-dihydroxybutyl]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxopropyl]amino]-5'-deoxythymidine (9CI) (CA INDEX NAME)

CM :

CRN 197431-10-0 CMF C41 H52 N8 O16 S2

1.4. 3.

Absolute stereochemistry.

PAGE 1-B

CM 2

CRN 25086-81-1 CMF (C10 H15 N2 O8 P)x CCI PMS

CM 3

CRN 365-07-1.

CMF C10 H15 N2 O8 P

Absolute stereochemistry.

Lymphokines

g. 1.1.14 (1977) (1987) (1987) (1987) (1987) ICM C07H021-00 IC ICS A61K047-48; A61K031-70; A61K038-55 CC 63-6 (Pharmaceuticals) Section cross-reference(s): 3 ΙT Nucleotides, biological studies RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (analogs and derivs., DNA containing; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses) Fatty acids, biological studies Polymers, biological studies Polysaccharides, biological studies Proteins, specific or class RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (conjugates, with nucleic acids; property-affecting and/or property exhibiting compns. for therapeutic and diagnostic uses) Fatty acids, biological studies RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (esters, conjugates with nucleic acids; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses) A. Carbohydrates, biological studies Macromolecular compounds RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ligands; property-affecting and/or property-exhibiting compasfor therapeutic and diagnostic uses) IT Peptides, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (nucleic acid targeting with; property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses) Cytokines Growth factors, animal Hormones, animal, biological studies

RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(property-affecting and/or property-exhibiting compns. for

therapeutic and diagnostic uses) IT Coenzymes Enzymes, biological studies Fibronectins RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses) IT 9004-10-8DP, Insulin, conjugates with oligo(T), biological -studies : RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses) IT 52123-30-5, L-Lysyl-L-lysine dihydrochloride 55750-62-4 68528-80-3, Suberic acid bis(N-hydroxysuccinimide) ester 195829-07-3 195992-88-2 195992-89-3 195992-90-6 197431-06-4 RL: RCT (Reactant); RACT (Reactant or reagent) (property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses) 195992-87-1P 195829-08-4P 195829-09-5P 195992-84-8P 195992-91-7P 197526-74-2P 197526-75-3P 197526-76-4P 197526-77-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (property-affecting and/or property-exhibiting compns. for therapeutic and diagnostic uses) ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN L32 ACCESSION NUMBER: 1994:650458 HCAPLUS Full-text DOCUMENT NUMBER: 121:250458 TITLE: Site-Specific Conjugation of a Engineered Protein Chilkoti, Ashutosh; Chen, Guohua; Stayton; AUTHOR (S): Patrick S.; Hoffman, Allan S. CORPORATE SOURCE: Center for Bioengineering, University of Washington, Seattle, WA, 98195, USA Bioconjugate Chemistry (1994), 5(6), SOURCE: 504-7 CODEN: BCCHES; ISSN: 1043-1802 DOCUMENT TYPE: Journal LANGUAGE: English A genetically-engineered mutant of cytochrome b5, incorporating a unique cysteine AB residue, was conjugated to maleimide-terminated oligo(N-isopropylacrylamide). The conjugation of the protein by reaction of the cysteine residue, precisely positioned by site-directed mutagenesis techniques, with an activated oligomer containing only one reactive end group in the oligomer chain permits the sitespecific and stoichiometric conjugation of the oligomer with the protein. The protein-oligomer conjugate was shown to exhibit lower critical solution temperature (LCST) behavior, similar to the free oligomer. Furthermore, the LCST behavior of the protein-oligomer conjugate is reversible and allows selective precipitation of the conjugate above its LCST. IT 157615-31-1 RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with site-specifically mutagenized cysteine-containing cytochrome b5, lower critical solution temperature behavior of conjugate in

relation to)

RN 157615-31-1 HCAPLUS

Cyclohexanecarboxamide, 4-[(2,5-dioxo-1-pyrrolidinyl)methyl]-N-[2-CN [[3-[(1-methylethyl)amino]-3-oxo-1-propenyl]thio]ethyl]-, homopolymer (9CI) (CA INDEX NAME)

· CM

157615-30-0 CRN CMF C20 H31 N3 O4 S

52-90-4, Cysteine, biological studies

RL: BIOL (Biological study)

(site-specifically mutagenized cytochrome b5 containing, conjugation) of oligo(N-isopropylacrylamide) with, lower critical solution temperature behavior of conjugate in relation to)

52-90-4 HCAPLUS RN

L-Cysteine (CA INDEX NAME) CN

Absolute stereochemistry.

CC 9-14 (Biochemical Methods)

157615-31-1 TΤ

> RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with site-specifically mutagenized cysteine-containing cytochrome b5, lower critical solution temperature behavior of conjugate in relation to)

52-90-4, Cysteine, biological studies IT

RL: BIOL (Biological study)

(site-specifically mutagenized cytochrome b5 containing, conjugation of oligo(N-isopropylacrylamide) with, lower critical solution temperature behavior of conjugate in relation to)

L32 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1992:251305 HCAPLUS .116:251305

DOCUMENT NUMBER: ,

Polyamine-linked Sepharoses: preparation and TITLE:

application to mammalian spermine synthase

Shirahata, Akira; Zhu, Chang Lie; Akatsu, Sakae; AUTHOR(S): Suzuki, Yasutoshi; Samejima, Keijiro

CORPORATE SOURCE:

Fac. Pharm. Sci., Josai Univ., Sakado, 350-02,

Japan

SOURCE .

1991), 2(4), 229-34

CODEN: PEXPEJ; ISSN: 1046-5928

DOCUMENT TYPE:

Journal

LANGUAGE: English

Seven different polyamine-linked Sepharose derivs. were prepared for the affinity chromatog. of spermidine and spermine binding macromols.: spermine synthase from rat and hog brain was used as a model protein with a spermidine binding site. Comparative studies of the affinities of the enzymes for the 7 matrixes suggested that 2 neg. charges, 3 to 4 methylene groups apart, should be present at the decarboxylated S-adenosylmethionine binding site and should improve the binding of the enzyme to the Sepharose derivative. Two neg. charges at the spermidine binding site would be expected to do the same. Three affinity matrixes linked with 1,17-diamino-4,9,14-triazaheptadecane, 1,21-diamino-4,9,13,18-tetraazaheneicosane, or 5-sperminecarboxylic acid had an affinity for spermine synthases higher than that of spermine-Sepharose, which has been used for the purification of spermine synthase. The first of these matrixes was used and proved to be effective for the purification.

IT 141255-06-3P 141255-11-0P

RL: PREP (Preparation)

(preparation of, for affinity chromatog. of polyamine-binding proteins)

RN 141255-06-3 HCAPLUS

CN Agarose, [6-[[4-[3-[[[5-amino-2-[(3-aminopropyl)amino]-1-oxopentyl]amino]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxobutyl]amino]hexyl]carbamimidate (9CI) (CA INDEX NAME)

CM 1

CRN 172723-80-7 CMF C23 H44 N8 O5 S

CM 2

CRN 9012-36-6 CMF Unspecified

CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 141255-11-0 HCAPLUS

CN Agarose, [6-[[4-[3-[[[2,5-bis[(3-aminopropyl)amino]-1-oxopentyl]amino]thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxobutyl]amino]hexyl]carbamimidate (9CI) (CA INDEX NAME)

CM. Street grafting high

CRN 172964-11-3 CMF C26 H51 N9 O5 S

CRN 9012-36-6

CMF Unspecified

CCI PMS, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 141136-49-4P 141136-50-7P

RL: PREP (Preparation)

(preparation of, for affinity chromatog. stationary phase preparation for polyamine-binding proteins purification)

RN 141136-49-4 HCAPLUS

CN Pentanamide, 2,5-bis[(3-aminopropyl)amino]-N-(3-mercaptopropyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 141136-50-7 HCAPLUS

CN Pentanamide, 5-amino-2-[(3-aminopropyl)amino]-N-(3-mercaptopropyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

化正式 医神经性囊肿瘤 医鼻囊炎

CC 9-3 (Biochemical Methods)

Section cross-reference(s): 7

TT 70356-67-1P 141255-06-3P 141255-07-4P 141255-08-5P 141255-09-6P 141255-10-9P 141255-11-0P

RL: PREP (Preparation)

(preparation of, for affinity chromatog. of polyamine-binding proteins)

141136-49-4P 141136-50-7P ΙT

RL: PREP (Preparation)

(preparation of, for affinity chromatog. stationary phase preparation for

polyamine-binding proteins purification)